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1. Rose, W. C. (1949), Amino Acid Requirements of Man, Federation Proc. 8:546, June.

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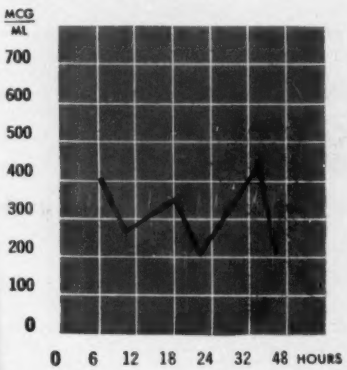

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2. Welch, H.; Hendricks, F. D.; Price, C. W., and Randall, W. A.: J. A. Ph. A. (Sc. Ed.) 39:185 (Apr.) 1950.
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NEUROAPPENDICOPATHY

Review of the Literature and Report on Fifty-Two Cases

NORMAN H. ISAACSON, M.D.
AND
BRIAN BLADES, M.D.
WASHINGTON, D. C.

APPARENT discrepancies between the clinical and anatomicopathological findings in appendicitis are only too familiar to both surgeons and pathologists. All too often a vermiform appendix is called normal by the surgical pathologist after a cursory examination of one or two sections stained with hematoxylin and eosin has failed to disclose inflammatory cells in the wall. In other cases the specimen is described as an "interval appendix" or a "chronic appendix," this description indicating a failure to discover the underlying disorder. In addition, there is great controversy among surgeons themselves on the subject of "chronic appendicitis." Many do not accept the diagnosis, believing that if an appendix is removed which shows no gross or microscopic evidence of inflammation the relief obtained, if any, is only mental.

There are no specific pathologic changes characteristic of the so-called chronic appendix. Symptoms referable to that organ can be produced by many extra-appendical causes,[1] by fecalith in the appendix, infestation with worms,[2] endometriosis,[3] kinks, and neoplasms of the appendix.

By far the commonest of the tumors of the appendix and probably the most frequent cause of the "chronic appendix" is the neuroma. As will be subsequently shown, it deserves to be considered as a clinical entity because of the symptoms it produces and the frequency of its occurrence. The title "neuroappendicopathy" is one coined by Simard [4] as descriptive of the syndrome and has been adopted here. It is preferable to the commoner term "neurogenic appendicitis," since in the usual case there is no evidence of active inflammation.

From the surgical and laboratory services, George Washington University Hospital.

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HISTORY

Though appendical fibrosis or obliteration of the lumen was long known and described, it was not until 1921 that "neurogenic appendicitis" was considered as an entity. In that year, Maresch [5] and Masson [6] independently observed that in many adults with a history of previous attacks of appendicitis there were narrowing of the lumen, diminution or absence of lymph follicles, thickening of the submucosa, hypertrophy of the muscles and hyperplasia of the periglandular nerve plexuses.

Schweizer [7] in 1922 presented five neuromas found in 12 patients with symptoms of chronic recurring appendicitis and added 15 more from routine autopsies of 20 patients with obliterated appendixes. In 1928 Urech [8] added 16 more cases, and subsequently further support was forthcoming from Rossle,[9] Schack,[10] Hosoi,[11] Simard,[4] Norgrore,[12] Fein, Hanan and Seidler [13] and Laird and Nolan,[14] until the literature at present contains reports of some 600 neuromas of the appendix.

Hoey [15] and Hosoi [11a] reported these lesions in patients suffering from von Recklinghausen's disease (multiple neurofibromatosis) in whom there developed symptoms of what was clinically similar to acute appendicitis.

Oberndorfer [16] reported ganglioneuromatosis in a huge appendix measuring 16 cm. in length. Similar cases have been reported by Schultz,[17] Peritz,[18] Poate

5. Maresch, R.: Über das Vorkommen neuromartiger Bildungen in obliterierten Wurmfortsätzen, Wien. klin. Wchnschr. **34**:181, 1921.

6. Masson, P.: Les lesions nerveuses de l'appendicite chronique, Compt. rend. Acad. Sc. **173**:262, 1921.

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10. Schack, L.: Der neuromuskuläre Apparat des Wurmfortsatzes bei der sogenannten chronischen Appendicitis (mit einem kasuistischen Beitrag zur Frage der Gallenblasenneurome), Beitr. z. path. Anat. u. z. allg. Path. **90**:392, 1932; Über die gelben Zellen in menschlichen Wurmfortsatz, Beitr. z. path. Anat. u. z. allg. Path. **90**:441, 1932.

11. Hosoi, K.: (*a*) Neurogenic Appendicitis: A Study of 195 Cases of Appendicular Neuromas, Am. J. Surg. **22**:428, 1933; (*b*) Neuromatosis of the Vermiform Appendix, Arch. Path. **16**:500 (Oct.) 1933.

12. Norgore, M.: Neuroma of the Appendix, Northwest Med. **35**:188, 1936.

13. Fein, M. J.; Hanan, J. T., and Seidler, V. B.: Plexiform Neuroma of the Appendix, with a Study of 600 Appendices, Am. J. Surg. **39**:27, 1938.

14. Laird, W. R., and Nolan, L. E.: Significance of Schwannomas as a Factor in Obscure Cases of Appendicitis, Am. J. Surg. **61**:418, 1943.

15. Hoey, T.: Von Recklinghausen's Disease Associated with Fibroma of the Appendix, Brit. M. J. **2**:490, 1928.

16. Oberndorfer, L.: Partieller, primärer Riesenwuchs des Wurmfortsatzes, kombiniert mit Ganglioneuromatose. (Ein Beitrag zur Entstehung der Ganglienzellen), Ztschr. f. d. ges. Neurol. u. Psychiat. **72**:105, 1921.

17. Schultz, A.: Ganglioneuromatose des Wurmfortsatzes, Zentralbl. f. allg. Path. u. path. Anat. **33**:172, 1922.

18. Peritz, L.: Zwei seltene Tumoren. Carotisdrüsentumor? Neurinom der Appendix, Zentralbl. f. Chir. **57**:2475, 1930.

and Inglis,[19] Lichtenstein and Ragins,[20] Schmincke [21] and Masson and Branch.[21a] Oberndorfer's case was discovered at routine autopsy; in all the other cases operation was performed after a mistaken diagnosis of acute appendicitis had been made.

PATHOGENESIS

When Maresch [5] and Masson [6] first described the tumors, they both believed that the growths arose in the same manner in which neural proliferations occur on

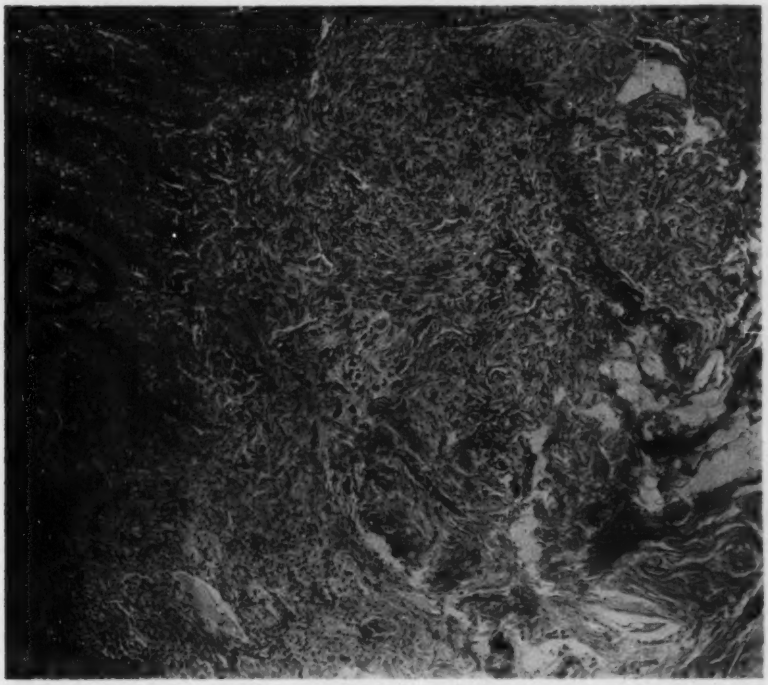

Fig. 1.—Appendix (× 45). This figure illustrates the method of formation of the neuromas. The argentaffin cells at the base of the crypts of Lieberkühn have migrated into the periglandular nerve plexuses, which in turn show proliferation.

the stumps of amputated nerves. The injury in this instance had occurred through division of the nerve filaments by an ulcerative or inflammatory process which was

19. Poate, H., and Inglis, K.: Ganglioneuromatosis of the Alimentary Tract, Brit. J. Surg. **16**:221, 1928.

20. Lichtenstein, B. W., and Ragins, A. B.: Ganglioneuroma of the Vermiform Appendix: Histologic Study of a Case, Arch. Path. **24**:788 (Dec.) 1937.

21. Schmincke, A.: Diffuse Neurinombildung in der Appendix. Kasuistische Mitteilung, Ztschr. f. d. ges Neurol. u. Psychiat. **84**:293, 1923.

21a. Masson, P., and Branch, A.: Gigantisme et ganglioneuromatose de l'appendice, Rev. Canad. de biol. **4**:219, 1945.

the cause of the obliteration of the appendical lumen. The effect on the nerves of the mucosa, they argued, would be the same as when they had been severed by instruments.

In subsequent papers,[22] however, Masson differentiated two types of neuromas. The first group are the ganglioneuromas, as reported by Oberndorfer and others [23] (see figs. 8 and 9). In these the proliferation begins in Meissner's plexus and extends to Auerbach's plexus. It is expressed by an increase in the number of nerves and usually of the ganglion cells also. Secondarily, it involves the mucous plexus, forming neuromas of slender fibers tending toward the upper layers of

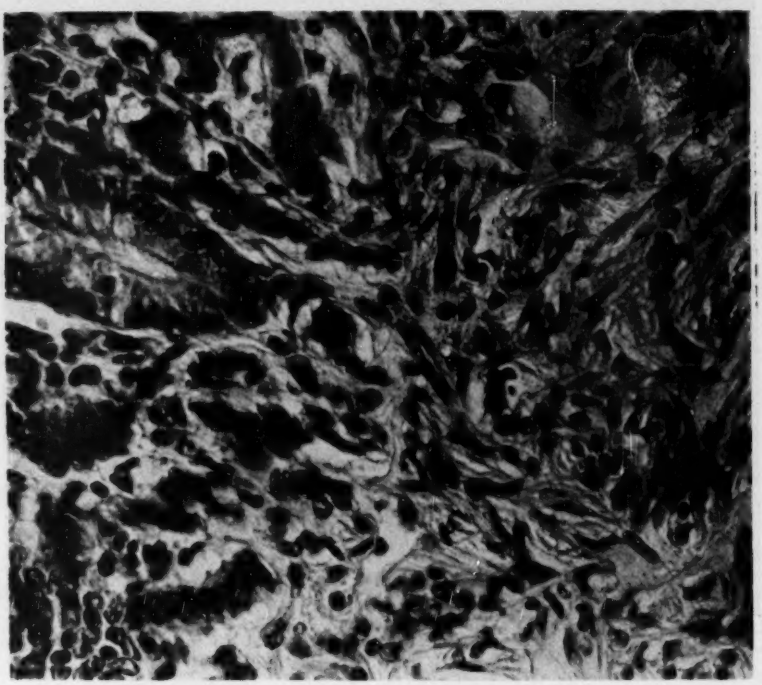

Fig. 2.—Appendix (× 200). Note the migrating epithelial cells, the interlacing bundles of nerve fibers. This patient was a 21 year old white man with a two year history of recurrent bouts of dull aching pain in the right lower quadrant of the abdomen accompanied with nausea and occasionally with vomiting.

---

22. (*a*) Masson, P.: Appendicite neurogène et carcinoïdes, Ann. d'anat. path. **1**:3, 1924; (*b*) Carcinoids (Argentaffin—Cell Tumors) and Nerve Hyperplasia of Appendicular Mucosa, Am. J. Path. **4**:181, 1928. (*c*) Masson, P., in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, pp. 1097-1130. (*d*) Masson, P.: Contribution to the Study of the Sympathetic Nerves of the Appendix: The Musculonervous Complex of the Submucosa, Am. J. Path. **6**:217, 1930.

23. Oberndorfer.[16] Schultz.[17] Peritz.[18] Poate and Inglis.[19] Lichtenstein.[20] Schmincke.[21]

the stroma. It is accompanied with hypertrophy, which may be enormous, of the muscular mechanism of the submucosa and the muscularis mucosae and secondarily of the arterial muscle and the muscular coat of the appendix. Such appendixes are thick, sometimes gigantic and have no tendency to involutional obliteration.

In the second and commoner group, only the deep region of the mucous plexus is affected, forming neuromas of large, nonmedullated fibers which push the muscularis mucosae outward but rarely pass beyond it. Masson [22d] has illustrated the fact that contemporaneous with slight irritation or inflammation the argentaffin

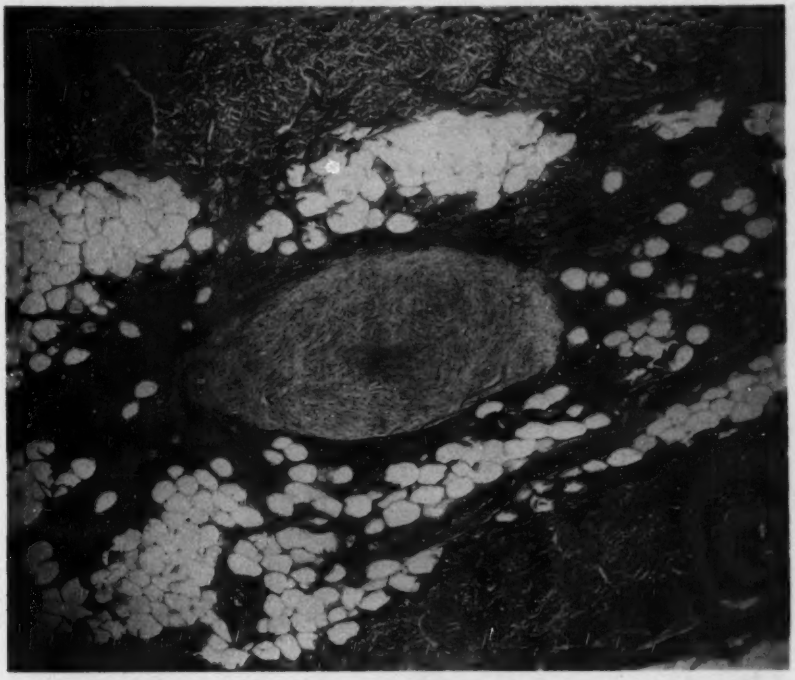

Fig. 3.—Appendix (× 45), showing a single neuroma in the center of the obliterated distal end. The patient was a 56 year old white man with recurrent pain in the right lower quadrant of the abdomen of such severity as to cause him to roll about in agony.

cells at the base of the appendical glands bud and emigrate into the periglandular nerve plexus (figs. 1 and 2). After this stimulus the nerves proliferate. These appendixes show a marked tendency to obliteration of their lumen. This type of neuroma survives the intestinal epithelium and increases in size with time. It can undergo degeneration, but if it does it is always after the disappearance of the argentaffin cells. In this type of neuroma the plexus of Meissner and Auerbach are intact. The emigration of the argentaffin cells, arising as offshoots of the crypts of Lieberkuhn, appears to be the primordial condition on which the development and persistence of the neuromas depend.

PATHOLOGIC CHANGES

There is nothing characteristic in the gross appearance of the appendixes to indicate the presence of such tumors. In a few cases the distal portion of the obliterated appendix is slightly enlarged in a fusiform or bulbous manner, but other benign tumors such as carcinoid, fibroma and myoma present similar enlargements. On section, the lumen of the majority of appendixes is partially or completely obliterated. Most of the neuromatous growths are microscopic in size. When grossly visible, the cut surface is gray-white and opaque.

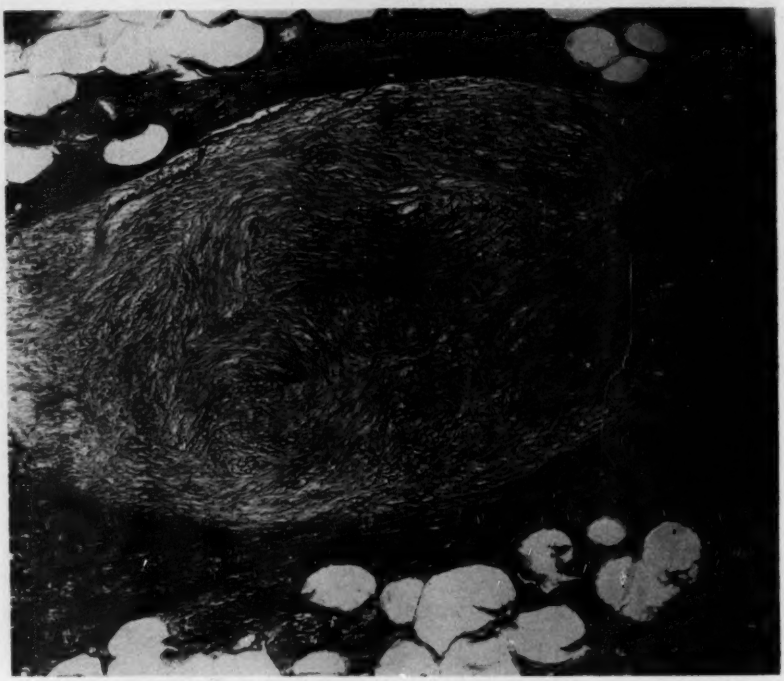

Fig. 4.—Appendix (× 98), showing details. Note the interlacing bands of neurofibrils and the palisaded nuclei.

For the study of microscopic sections in the identification of neuromas, the Masson trichrome stain [22b] is best. Often minute groups of neuromatous tissue will escape detection when other staining methods are used. If the sections are properly stained, the Masson method quickly picks out and identifies the neuromas as red, loosely anastomosing strands of nonmedullated nerve fibers or as red islands of compact interlacing bundles lying in a field of blue-staining fibrofatty tissue composing the axial core of the obliterated appendix (figs. 3 and 4). Whenever the muscularis mucosae is intact, the neuromas are seen to be central to it.

Fig. 5.—Appendix (× 91) showing a multiplicity of neural proliferations in the obliterated portion. The patient was a 22 year old Negro whose appendix was removed during his third attack of pain in the right lower quadrant of the abdomen, nausea and vomiting.

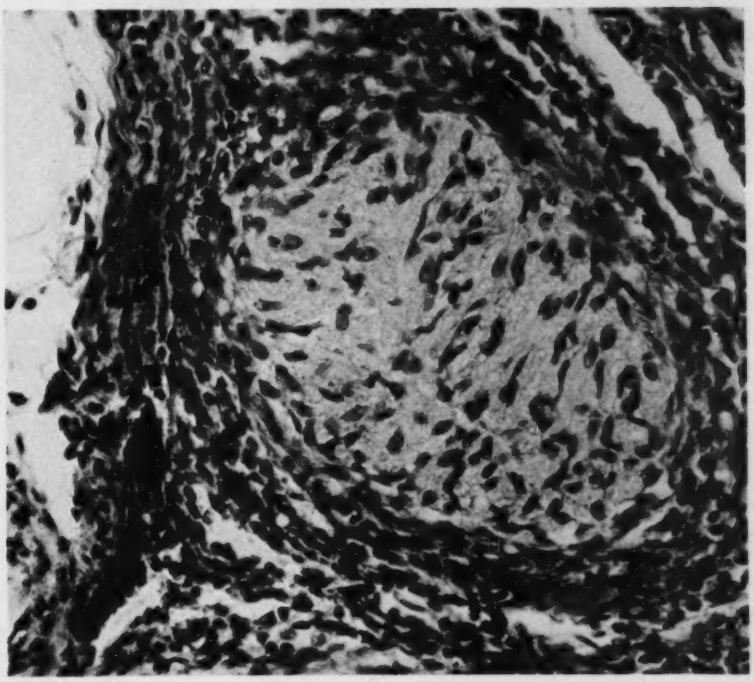

Fig. 6.—High power magnification (× 355) showing details of one of the neuromas.

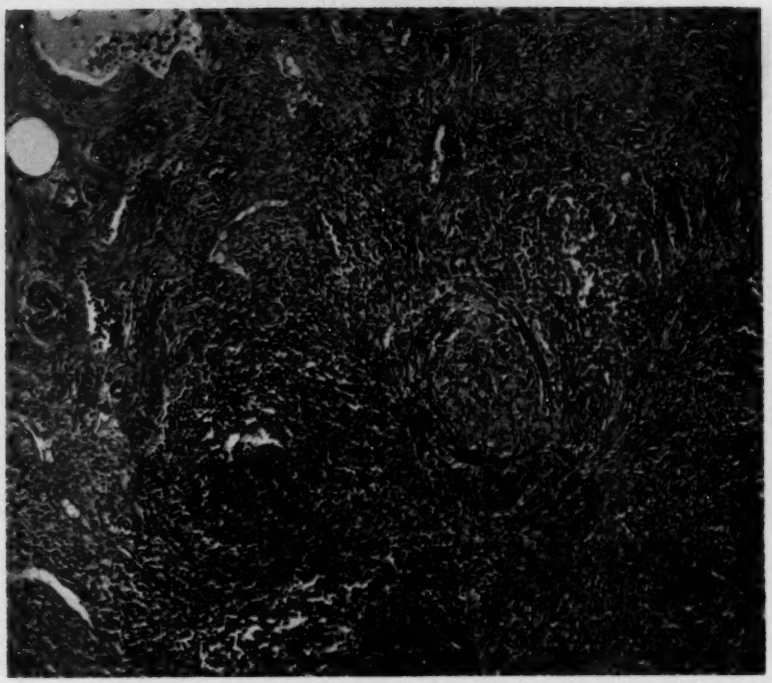

Fig. 7.—Appendix (× 45), showing a small circumscribed neuromatous nodule in the obliterated tip. The chronic inflammatory cells are regarded by Masson as indicative of regression of the neuroma. The patient was a 24 year old white man with a history of recurrent dull pain in the right lower quadrant of the abdomen without nausea or vomiting.

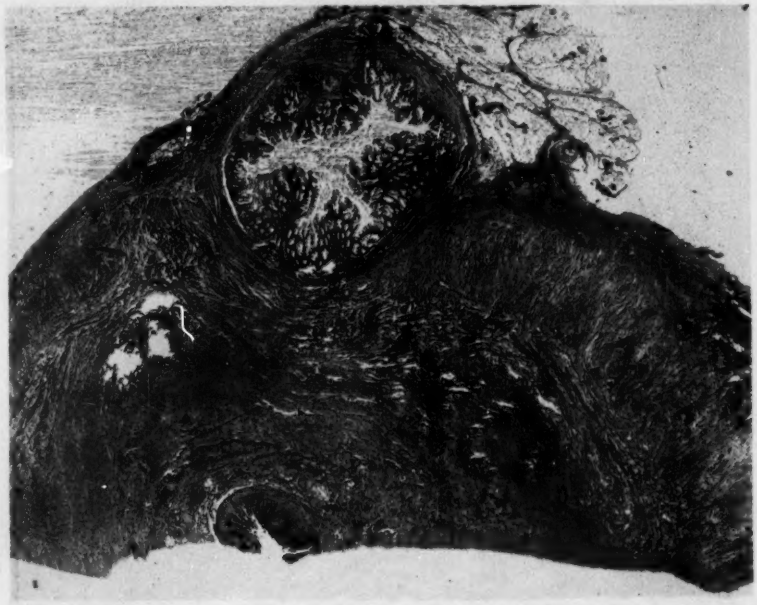

Fig. 8.—Ganglioneuroma of the appendix (× 7). Note the marked thickening of the wall of the appendix, which measured 1.5 cm. in width. The patient was a 34 year old woman complaining of intermittent pain in the right lower quadrant, "like childbirth," for a year Pain was constant and severe enough to confine the patient to bed for 11 days prior to operation.

They rarely break through the muscularis mucosae and extend into the submucosa. The number of neuromas varies from one to many. When multiple, they are linked together by many nerve fiber strands, stretching from tumor to tumor like telephone wires (figs. 5 and 6). These neuromas contain a variable admixture of argentaffin cells or lymphocytes. Masson considers the presence of lymphocytes a sign of retrogressive change [22b, d] (fig. 7). When sections are treated with silver stains, it is observed that the nonmedullated fibers are supported by a lacy network of fine reticulum having an intricate honeycombed appearance.

Fig. 9.—Ganglioneuroma of the appendix (× 130). Note the interlacing strands of neural tissue and the clumps of ganglion cells.

By contrast, the ganglioneuromas described in the literature [23] were all gigantic appendixes with pronounced thickening of the walls. Some of them were large enough to be palpated abdominally. Associated with a rich number of nerve fibers, there are extraordinary huge masses of ganglion cells, which in Oberndorfer's case [16] were arranged in groups that were visible macroscopically in stained sections. The ganglion cells are those of Meissner's and Auerbach's plexuses which have undergone considerable hyperplasia. Occasionally there also is involvement of the mesoappendix in these cases (figs. 8 and 9).

MATERIALS AND METHODS

Incidence.—A study was undertaken of 75 appendixes surgically removed because of clinically manifest "appendical" symptoms. In all cases routine hematoxylin and eosin stains were done and the report of "no pathological diagnosis" or "fibrosis of appendix" had been made. The specimens were removed by a number of surgeons operating at George Washington University Hospital, no one surgeon predominating. With the use of multiple sections of these appendixes (usually six to eight) and the Masson trichrome stain, 24 neuromas were found in the group, an incidence of 32 per cent. Other authors,[24] after similar studies, have reported an incidence of 34 to 56 per cent, depending on the number of sections taken. The neuromas were not limited to the fibrosed or obliterated appendixes as some authors state,[25] though the incidence with this type of appendix was 64.3 per cent, as compared to 24.6 per cent for the "normal appendixes" in the study and 75.2 per cent in Simard's series.[4] Why, then, is the diagnosis not made oftener? In the routine study of appendixes, most pathologists are content with one longitudinal and one cross section of the appendix stained with hematoxylin and eosin. These tumors are frequently minute and present only in a limited number of sections. The large number of cases found in the literature were discovered only when multiple or serial sections of the appendix were done. Furthermore, many authors [26] have stressed the inadequacy of hematoxylin and eosin in the identification of minute neuromas. The Masson trichrome technic [22b] of staining the same sections quickly identifies the red neuroma, frequently masked in the hematoxylin and eosin preparation, where it is often interpreted as cicatricial tissue. If a sufficient number of sections taken at intervals throughout the appendix were examined with the Masson stain, the diagnosis of neuroma would be made more frequently and that of "normal appendix" or "fibrosis of appendix" would be less common.

RESULTS

The Clinical Picture.—To the 24 cases discovered by the method described 14 cases were added from the pathology files of the George Washington University Hospital and 14 from the files of the Armed Forces Institute of Pathology. The latter groups had been discovered on routine hematoxylin and eosin preparation. Five of the patients had their appendixes removed at routine gynecologic operations, but, on questioning, they described symptoms in their past history similar to those of the group as a whole. Two patients had their appendixes removed during the course of cholecystectomy. They were excluded from the analysis of the symptomatology of "neuroappendicopathy" because their concomitant gallbladder disease tended to overshadow any symptoms referable to the appendix.

Age.—The age incidence in this series ranged from 15 to 71 years. Ninety per cent of the patients fell in the age group 20 to 50. In cases reported in the literature the ages have ranged from 8 to 79.[11a]

Sex.—There were 30 females in this group and 22 males. Females predominate in the reported literature also, in some series as much as 3 to 1.

Race.—There were 49 white and 3 Negro patients, a relative proportion roughly equivalent to the patient population at George Washington University Hospital.

Symptomatology.—The symptoms were analyzed in 50 cases, exclusive of the two in which gallbladder disease was also present.

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24. Dordick, J. R.: Diverticula of the Vermiform Appendix Associated with an Overgrowth of Nerve Tissue and a Partial Mucocele, Arch. Path. **27**:735 (April) 1939. Hosoi.[11a] Simard.[4] Fein, Hanan and Seidler.[13]

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26. Masson.[6] Hosoi.[11b] Fein, Hanan and Seidler.[13]

Pain: In 46 cases (92 per cent) the pain was described as a dull ache in the right lower quadrant, or the terms "soreness," "gnawing," "burning," "discomfort" or "cramping" were used. The pains were constant, intermittent or periodic. Occasionally they began as acute pains which were generalized throughout the abdomen or started in the epigastrium, umbilical region or right lower quadrant, to be followed by a dull ache in the right lower quadrant, which was then constant in duration. In 4 cases the pain was described as severe, knifelike, stabbing or griping in character. In one case it was so intensely severe that the patient would double up or roll about in agony.

Careful questioning of the patients revealed that 45 (90 per cent) of them had had previous similar attacks. These attacks varied in number and extended over a period of two weeks to 15 years. They recurred at intervals of two weeks to four years. The pain on previous occasions (as well as the other symptoms) either disappeared spontaneously or with the help of ice bags to the abdomen and/or analgesics.

Nausea and Vomiting: One or the other of these symptoms was present in 28 cases (56 per cent). Four additional patients complained of anorexia, "indigestion" or epigastric distress.

Change in Bowel Habits: Four patients complained of diarrhea. Eight complained of associated constipation.

Physical Findings: There was minimal to moderate tenderness in the right lower quadrant in 42 cases (84 per cent), most frequently at McBurney's point. In eight cases (16 per cent) no abdominal tenderness was elicited. Rebound tenderness was present in the right lower quadrant in six cases (12 per cent).

Muscular spasm was present in the right lower quadrant in five cases (10 per cent) and was classified as minimal in all. Two additional patients had moderate rigidity of the right rectus area.

Rectal examination was recorded in 10 cases and was noncontributory in nine of these. One patient had some tenderness on the right. Positive psoas and obturator signs were recorded in one case.

The temperature was normal in 46 cases (92 per cent). Four patients showed an elevation, which did not exceed 37 C. (100 F.). The pulse rate was between 60 and 80 in 35 cases (70 per cent), between 80 and 90 in 10 cases (20 per cent) and between 90 and 100 in 5 cases (10 per cent). The respirations were usually normal. The white blood cell count was normal in 41 cases (82 per cent). Nine patients had counts ranging from 11,000 to 16,000, but differential counts were normal in all but one of these.

In three cases gastrointestinal roentgenograms and those made after barium enemas were reported as normal. Intravenous and retrograde pyelograms were normal in two cases. Blood urea nitrogen and nonprotein nitrogen were recorded as normal in one case.

The recurrent nature of the symptomatology was evident in the recorded preoperative diagnoses. In 31 cases the impression was "chronic" or "recurrent" appendicitis; "subacute appendicitis" was diagnosed in 3 cases and acute appendicitis in 11 cases. In five cases in which the appendix was removed in the course of a gynecologic procedure, no diagnosis referable to the appendix was recorded.

Prognosis.—Follow-up reports were obtained in 23 cases by means of a mailed questionnaire. In 22 of these there has been no recurrence of symptoms after

periods ranging from four months to two years following the operation. In the one patient who failed to obtain relief, no cause for her continued symptoms has been found as yet. Laird and Nolan,[14] after a similar follow-up of 14 patients, reported complete relief in 13.

At this point it would not be amiss to point out that symptomatic neuromas occur elsewhere in the gastrointestinal tract as well. Stoerk [27] reported the case of a patient who had undergone a gastrojejunostomy for gastric ulcer, with no relief of symptoms. Two years later the gastric ulcer was resected, and microscopic examination showed neuromatous proliferation, the structure of which was very much like that of amputation neuromas. Askanazy [28] reported three similar lesions, one of which contained ganglion cells as well as proliferated nerve fibers. He called them "scar neuromas" and felt that to a certain extent they may be the cause of gastralgias. Okkels,[29] in a study of serial sections of 34 gastric ulcers, found that the nerves were increased in number and size, running in all directions, and that enormous masses of nerve tissue were present in the ulcerated gastric wall. Hamperl [30] reported similar tumors in the gallbladder.

SUMMARY AND CONCLUSIONS

Neuromas are not unusual in the appendix and probably are the cause for the removal of a large number of so-called chronic appendixes. Two types of neuromas are present here, the commoner axial or plexiform neuroma which arises from the periglandular nerve plexuses usually after migration of argentaffin cells into this area and the rather rare ganglioneuroma which arises from Meissner's and Auerbach's plexuses.

"Neuroappendicopathy" is a distant entity. It usually produces a dull ache or discomfort in the right lower quadrant, with slight tenderness at McBurney's point. Nausea with or without vomiting may be present. The condition can produce pain so severe as to cause patients to roll about, and physical examination may reveal severe tenderness and abdominal muscle spasm.

In spite of the apparent acuteness of symptoms and signs, the temperature is usually normal and the total white and differential cell counts tend to remain at normal levels. Careful questioning most often reveals a history of previous attacks.

Fifty-two cases of the syndrome are reviewed, and figures demonstrating the microscopic changes are shown. Before an appendix is considered normal in a patient with symptoms referable to the appendix, multiple sections stained with the Masson trichrome technic should be examined. As the diagnosis becomes commoner pathologically, ability to evaluate the clinical symptomatology of the condition will increase. Only in this way may we hope to gain precision in diagnosis and to differentiate similar conditions arising not only in the appendix itself but in other portions of the body.

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CLINICAL SIGNIFICANCE OF THE CONTACT-COMPRESSION FACTOR IN BONE SURGERY

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THE TREATMENT of fractures by the application of methods and principles thought to be concomitant with the physiology of bone repair has created many divergent opinions. The disagreement is the result of the many complexities involved in securing osseous union. Bone is one of the few body structures which for normal function requires the reconstruction of the cellular detail present in the normal mature structure. The usual healing of many of the so-called soft tissues is by fibrous tissue. The healing of bone is accomplished my metaplasia of the anaplastic cells, with mineral depositions forming a structure identical to the original bone in character and constitutional elements. This complex process is influenced by many factors, chemical and physical, about which we must learn more.

The importance of the physical forces in fracture healing was impressed in our experiences when over a period of years many ununited fractures were examined. The fractures had been treated by surgical methods with metal fixation, and nonunion of the fractures frequently resulted. The fixation was as rigid as mechanically possible, and the technic for such methods was correct. The observation was made that if the metallic apparatus were removed in these cases of rigid fixation with nonunion and then a cast or properly controlled traction were applied as for a closed reduction, the fractures would unite.

Since no alteration of the basic physiology was created in these cases, it was presumed that the factor was a physical one. This factor was considered not merely to be one of contact of the fractured ends but to include the muscular forces compressing the fracture surfaces in longitudinal and transverse directions. In order to treat a fracture surgically and retain the muscular forces and their influences on the contacting surfaces, a slotted type of plate was designed (fig. 1) which could be applied to the shaft of the fractured bone and thus allow the fractured ends to be under the same physical forces of contact and compression as are present in the closed reduction. Thus, the fractured ends could oppose

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viable bone as the devitalized bone of the fractured portion was absorbed. The slotted plate was named "contact splint," because it permitted longitudinal motion and insured constant contact. The splints were applied snugly, but the screws were not tight and, thus end to end compression was permitted (fig. 2). The splint was designed long enough to convert all shearing forces into compres-

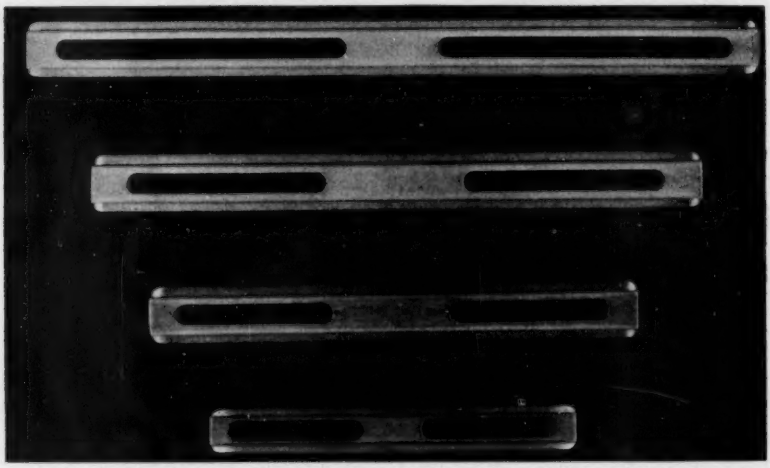

Fig. 1.—Contact splints, 6, 5, 4 and 3 inches (15.3, 12.7, 10.2, 7.6 cm.) in length.

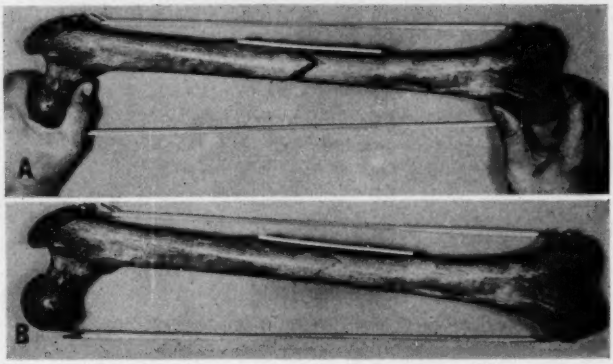

Fig. 2.—*A*, contact splints on femur. Rubber bands simulating longitudinal muscular pull. Traction shows how fragments will separate because the splint is not rigidly fastened. Such distraction is prevented at operation by proper screw placement. *B*, the traction has been released, and the longitudinal pull with the rubber bands opposes the fractured ends and maintains them in apposition with contact-compression during the healing period.

sion forces. The clinical use of the contact splint soon verified the theory of the physical influences on fractured bone. The shaft fractures which required internal fixation when subjected to the application of the contact splint promptly healed (fig. 3). Our conviction was that such a device permitted contact and compression forces to act in a physiological manner and help secure bony union.

An interesting observation was made on the shafts of transverse fractures of the femur treated with the contact splint. The primary purpose of the contact splint was to maintain and secure contact of the viable portions of fractured ends as the devitalized zone was absorbed. Teleoroentgenograms were made, and by careful measurements of fixed points the amount of absorption of the devitalized bone was to be determined. To our amazement, there was no loss of bony length by absorption of the devitalized fractured ends. The explanation for this observation remained unsolved until in the experimental work on rats we observed that where pressure was not excessive absorption and osteogenesis occurred concurrently, thus achieving a physiological balance of some merit. The experimental work will be mentioned.

Apparently supported only by clinical observations, the proved value of the contact-compression factor remained a theory. To test with adequate controls the hypothesis that such a factor had a favorable influence on osteogenesis, experiments were considered on laboratory animals. It was rather difficult to secure in a mammal an osseous structure free from extraneous forces. The tibia, fibula and femur of the usual laboratory animals could not be used because of the forces exerted by the animals standing or lying on the part, and in a removal of the

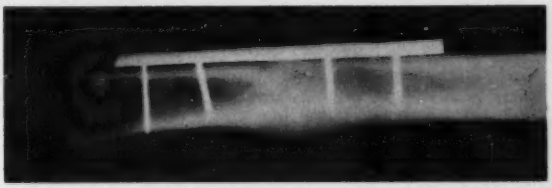

Fig. 3.—Oblique fracture of femoral shaft with contact splint applied. Ten months after operation complete bony union and improved contact due to muscular forces compressing the fractured ends can be seen.

musculature the circulatory factor would be altered. The bone found available was the parietal bone of rats, which is free from weight bearing, and muscular attachments and is accessible for study. The details of the experimental work have been previously recorded, and it will be sufficient to mention the basic principles.

A rectangular flap was cut in the parietal bone of the rat, with three margins free and the base attached to retain the blood supply (fig. 4). As shown in the diagram, the flap margins could be placed in contact and compression on either the medial or the lateral side as desired. The small flap created distal to the experimental flap was in all cases a control area. Thus, in each animal a flap could be obtained with one margin under contact and compression and compression without contact, while these forces were absent on the other margin. The distal flap was a control because there was no contact-compression factor applied. The width of the flap was nearly 1,500 microns, and thus in the lower power of the microscope one could see in serial sections the result of the forces applied. The area is so small that physiological conditions are as nearly identical as possible.

The results of the flap marginal compression were informative. The side of the flap under the contact-compression factor united and showed the effort to unite across gaps in the bone margins, and the margin not compressed did not unite. By applying the pressure on the medial or lateral side, osteogenesis and

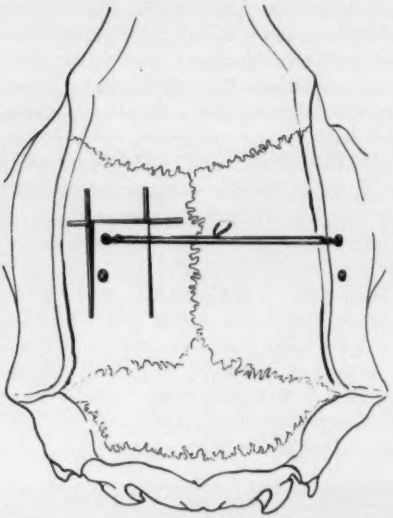

Fig. 4.—Rectangular flap showing contact-compression factor applied to the skull of a rat. Alternate compression point indicated by extra drill holes. (Reproduced with permission from Eggers, G. W. N.; Shindler, T. O., and Pomerat, C. M.: The Influence of the Contact-Compression Factor on Osteogenesis in Surgical Fractures, J. Bone & Joint Surg. **31-A**:693-716, 1949.)

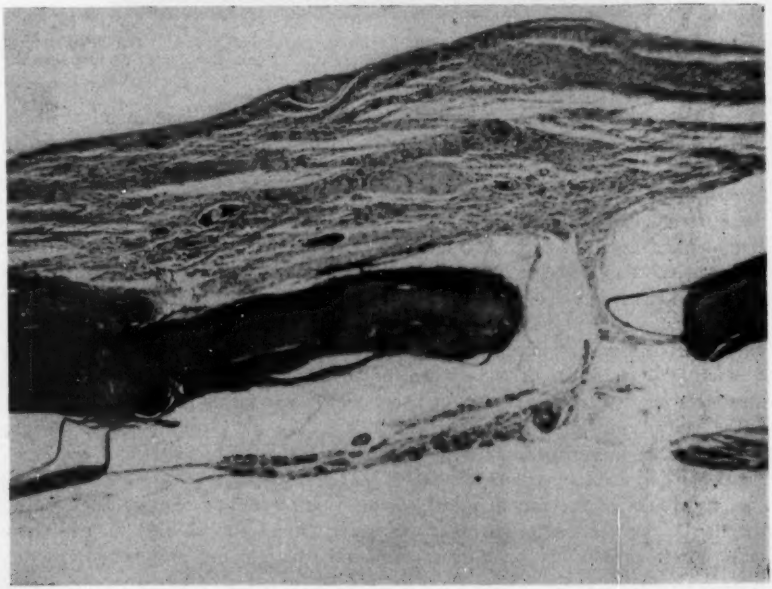

Fig. 5 (20 days; × 90).—Contact-compression factor applied on lateral side. Osteogenesis is present on lateral side but not on medial side.

union could be secured as desired. If the contact-compression factor were omitted, neither margin united. Therefore, because the only variant in the experiments

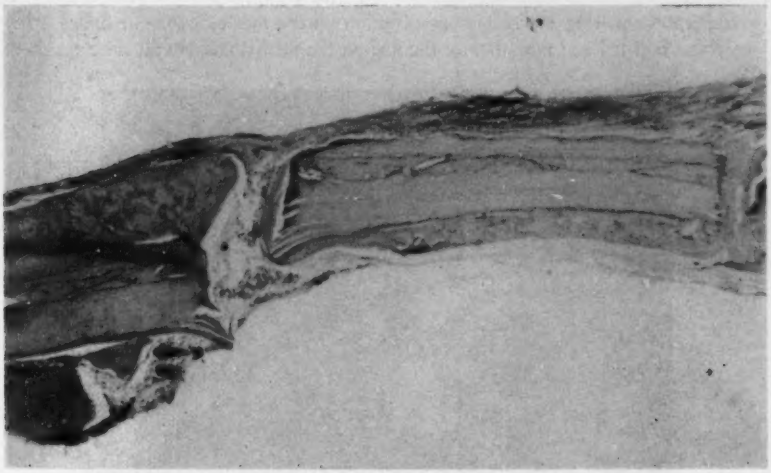

Fig. 6 (39 days; × 90).—Contact-compression factor applied to medial margin.

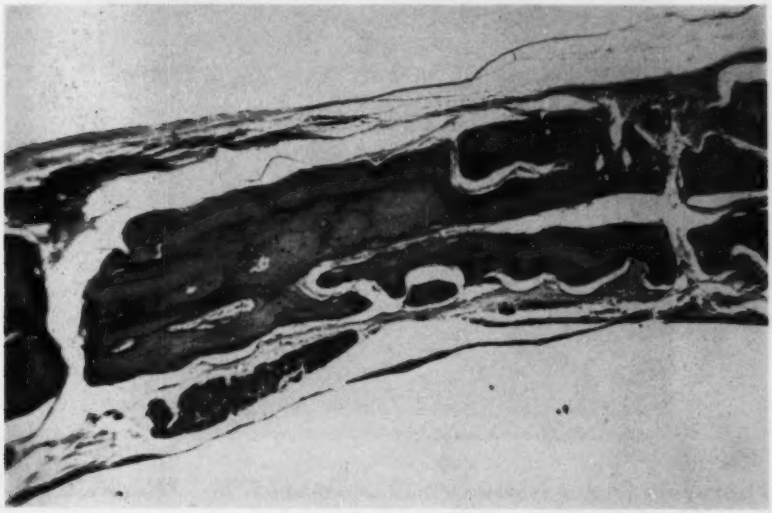

Fig. 7 (94 days; × 90).—Contact-compression factor omitted. No union of either medial or lateral saw cut.

appeared to be the contact-compression factor, it was concluded that this force favored osteogenesis and corresponded to forces which act favorably on the fractured ends of long bone.

Figure 4 shows the method of applying the compression by small hooks and split rubber bands. Figure 5 shows the application of compression for 20 days on the lateral side, with osteogenesis on the compressed margin. Figure 6 demonstrates securing osteogenesis and union on the medial side. In figure 7 the factor was omitted and nonunion of the flap on the medial and lateral sides resulted.

Fig. 8.—Chip graft fusion of vertebrae four years postoperatively. Note response of grafted bone to compression.

Thus, we were able to produce nonunion experimentally by omitting the contact-compression factor which resembles clinical nonunion.

The experience of adapting the contact-compression factor in osseous surgery has convinced us that it is a desirable physical force. Solution of such problems as arthrodesis by compression, the alteration of the shelf in hip operative procedures, excess bony proliferation on articular margins and grafting of bone by muscular pressure retention of the graft against the recipient bony surface require

adaptations of the contact-compression factor. Fractures should be treated so as to utilize the principle whether one uses surgical fixation by the contact splint, the intramedullary nail, the obliquely inserted Smith-Petersen nail or any other surgical method or if the time-proved closed reduction is followed. Shearing forces must be converted into pressure forces for good results. Fractures in children deserve special mention because operative treatment of them is rarely indicated.

Fig. 9.—Tuberculosis of knee with draining sinus. Eighteen months after operation there is bony union. Sinus promptly healed

Closed reduction which utilizes the contact-compression factor and is associated with growth will result in satisfactory recovery.

The contact-compression factor when adapted to osseous surgery will create or improve a successful procedure. The vertebral fusion in scoliosis should be greatest on the concave side (fig. 8) because the pressure will result in a stronger, firmer structure of the grafted bone due to internal and external reconstruction as

recorded by Julius Wolff over sixty years ago. Bone responds to added physical responsibility by a slow, gradual hypertrophy of the structures.

Figure 9 shows a fusion of the knee joint by compression, and the favorable reaction of cancellous bone to the factor is obvious. The proliferation of joint margins as in arthroplasties of the hip reminds us to decrease these areas at operation to allow for anticipated osteogenesis.

The presence and value of the contact-compression factor should be constantly evaluated in anticipated bone operations. If the procedures will deprive the parts of the factor, poor results can be anticipated; if the factor is utilized to its fullest extent, favorable effects can be expected.

The healing time for osseous union proceeds in an orderly physiological sequence when a favorable contact-compression factor is present; we cannot say the process is hastened, but it is not retarded.

It is our sincere conviction that any method of rigid fracture fixation, arthrodesis or grafting of bone which deprives the area treated of the contact-compression factor denies the parts of a necessary and useful physiological influence. The degree of compression is not definitely known, but that which is exerted by the normal musculature is considered as being the most favorable physiological pressure. No doubt it is variable. We are convinced of two facts, namely, that too much pressure causes bony necrosis and the absence of the contact-compression factor is conducive to nonunion.

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EXPERIMENTAL STUDY OF THE EFFECT OF PRESSURE ON THE HEALING OF BONE GRAFTS

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THE QUESTION as to whether or not pressing the fragments together exerts a beneficial influence on the union of two apposed fragments of bone is one which has concerned orthopedic surgeons from time to time. In 1932 Key [1] described a method for arthrodesing the knee in which the bone ends were positively pressed together and in which the pressure was maintained until the fragments were firmly united. It was believed that this resulted in more rapid union than had been obtained by any other method. The method has also been used by Charnley,[2] who reported on a series of patients treated by positive pressure in which successful arthrodesis of the knee was obtained in an unusually short time.

The contact splint introduced by Eggers [3] uses the tone of the muscles to maintain apposition of the fragments and actually to press them together. He believes that with the use of his method of internal fixation fractures of long bones unite more rapidly and with more certainty than they do when treated by other methods.

In a recent paper Eggers, Shindler and Pomerat [4] described some experiments in which, by means of saw cuts, linear fractures were made in the skulls of rats. Then by elastic bands the edges of the saw cuts were approximated in one situation while they were slightly distracted in an adjacent parallel cut. Where the margins of the saw cuts were pressed together they united promptly by bone, but where they were slightly distracted, and also in nearby control cuts where no pressure or distraction was used, bony union did not occur even after 91 days.

Over 20 years ago one of us (J. A. K.) attempted to determine the effect of positive pressure on the union of experimental fractures in animals, but the results were inconclusive and were not published. We are impressed by the fact that bony

From the Department of Surgery, Washington University School of Medicine.

Read before the Section on Orthopedic Surgery at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

1. Key, J. A.: Positive Pressure in Arthrodesis for Tuberculosis of the Knee Joint, South. M. J. **25**:909-915 (Sept.) 1932.

2. Charnley, J. C.: Positive Pressure in Arthrodesis of the Knee Joint, J. Bone & Joint Surg. **30-B**:478-486 (Aug.) 1948.

3. Eggers, G. W. N.: Internal Contact Splint, J. Bone & Joint Surg. **30-A**:40-52 (Jan.) 1948.

4. Eggers, G. W. N.; Shindler, T. O., and Pomerat, C. M.: The Influence of the Contact—Compression Factor on Osteogenesis in Surgical Fractures, J. Bone & Joint Surg. **31-A**:693-716 (Oct.) 1949.

union did not occur in the controls in the experiments of Eggers, Shindler and Pomerat and recall that fibrous union is not uncommon in skull fractures. We wondered whether their experimental results would be true of other bones where bony union is to be expected. Consequently some experiments were performed on the iliac bones of dogs. In some of these, experimental fractures somewhat similar to those of Eggers, Shindler and Pomerat were produced and subjected to pressure. The results of these will be reported elsewhere. In this paper we shall report observations on the healing of autogenous rib grafts to defects in the ilium. On one side the rib graft was flexed and its ends sprung into drill holes in the ilium and its position under strong pressure was maintained by its own elasticity, while on the

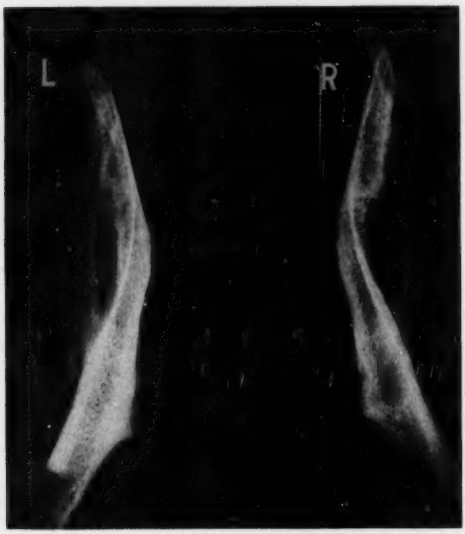

Fig. 1.—Roentgenogram of each ilium of dog 46 eight weeks after operation shows the manner of insertion of the rib grafts. The rib on the left was tightly inserted into two oblique drill holes, under pressure. The rib on the right side was placed in a drill hole at the base of the ilium and allowed to lie loosely in a notch at the upper end, without pressure.

other, or control, side the graft was placed in a drill hole and trench without pressure and its position was maintained by suturing the soft tissues over it (fig. 1).

METHOD

With the observance of aseptic conditions and with the animal under complete anesthesia induced with pentobarbital sodium sections of the lower two ribs on one side were removed subperiosteally and one was transplanted into each ilium with the convex surface facing outward. The rib grafts were about 2 inches (5 cm.) long. On the left side two holes were drilled obliquely through the ilium. They were so positioned that one end of the rib graft could be placed in one hole and then by slightly flexing the graft the other end could be forced or sprung into the other hole. This required considerable force, and when the graft was in position its own elasticity held it firmly in place and exerted considerable pressure on the adjacent portions of the ilium.

On the right side a similar hole was drilled obliquely in the posterior portion of the ilium and a groove was cut in the anterior portion. These were so positioned that when one end of the graft was placed in the hole the other end rested in the groove without undue pressure. This graft was laid loosely in position with the convex surface outward and its position was maintained by suturing the soft tissues over it.

Eight dogs were used and were killed at one, two, three, four, five, six, eight and nineteen weeks, and in each the pelvis with the grafts in place was excised and preserved in formaldehyde. Later the excess soft tissue was removed and the experimental area with the graft in place was excised from each ilium with a saw and the specimen examined roentgenologically. Then on the left side where the graft had been sprung into place, the section of ilium between the ends of the graft was cut across in order to determine whether the elasticity of the graft was still sufficient to separate the fragments of the ilium. In no case was there sufficient elasticity. Consequently the pressure which the ends of our grafts exerted on the adjacent bone must have decreased considerably within a few days after the graft was sprung into position.

Each rib graft was then cut across near its middle with a saw, and a small cross section was removed for microscopic examination. The excess bone was then removed from the ilium around the ends of the grafts and the specimens were decalcified and sections prepared and stained with hematoxylin and eosin. The blocks were so oriented that we obtained a cross section of each graft near its middle and a longitudinal section of each end of each graft and the adjacent portion of the ilium with the graft in place. These sections were cut in such a manner that the graft was cut longitudinally with the section passing through the ilium at right angles to its surface.

OBSERVATIONS

Gross Appearance.—Examination of gross specimens at autopsy revealed that on the left, or pressure, side the ends of the bone were firmly embedded in the holes in the iliac bones and appeared to be firmly fixed there even at one and two weeks. On the right, or nonpressure, side the ends of the grafts appeared to be fixed only by fibrous tissue at one and two weeks. In the specimens removed at the end of three weeks and at longer intervals the ends of the grafts appeared to be united to the ilium by bone.

It is thus noted that during the first two weeks the grafts on the pressure side were more firmly fixed to the ilium. This is what we would expect, but it does not indicate that clinical bony union was present at this time. At three weeks and later, bony union was present on each side, and this became progressively more firm in the experiments of longer duration. There was no perceptible difference between the pressure and the nonpressure grafts.

Roentgenographic Appearance.—In roentgenograms the relation of the ends of the grafts to the ilia was revealed, and in each instance it was satisfactory. As stated, on the pressure side the rib ends were embedded in holes in the ilium and on the nonpressure side one end was embedded in a hole in the ilium and the other end lay in the slot in the ilium.

New bone first made its appearance on the outer surface of the ilium adjacent to the graft. It was visible in all the specimens in which the experiment lasted three weeks or longer. The roentgenograms showed what appeared to be clinical union by bone on each side at four weeks and in all older specimens. We could not detect any difference between the pressure and the nonpressure sides.

We had hoped that roentgenograms of the ribs on the pressure side would reveal hypertrophy in response to compression strain and thus indicate viability and response to function in the graft. This did not occur, and the roentgenogram revealed no difference in the ribs on the pressure and nonpressure sides in the later experiments.

Microscopic Changes.—Pressure Side: In all the sections which included the junction of the graft and the host bone there was evidence of union of the two (fig. 2) by new bone, and in every instance in which the origin of the new bone could be identified it arose from the host bone. We were not able to detect any growth from the graft. Not only did the graft die and its lacunas become empty, but this change also occurred in a rather wide zone around the hole in the cortex of the ilium where it had been drilled for the reception of the graft. At the end of one week the superficial lacunas of the graft were empty, and in the sections taken from a rib removed two weeks after operation only a few of the lacunas in the depths of the compact bone contained pyknotic nuclei.

The marrow in the rib grafts as well as the tissue in the haversian canals was practically all dead in the one week specimen. An occasional cell or small group of cells in a haversian canal near the surface of the graft appeared to be living, but we

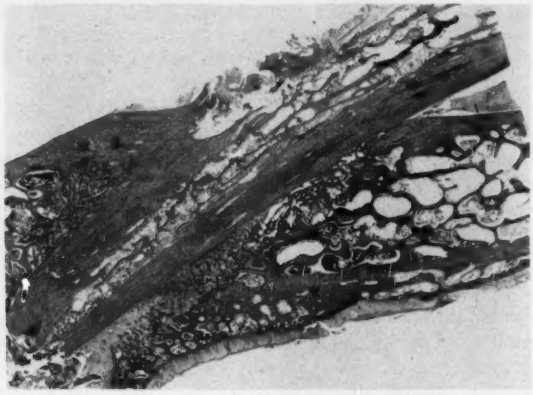

Fig. 2 (× 5).—With pressure. Sagittal section through the rib graft one week after operation at the site of its insertion in the ilium shows the graft well embedded in the host. New bone has begun to form inside the host. Viable fibrous tissue is present in the end of the rib. The absence of the outer cortex of the rib is an artefact. No new bone is present at the points of maximum pressure.

could not be sure of this and saw no evidence that any of these cells produced new bone or contributed to the union of the graft with the host.

Absorption of the rib graft by osteoclasts had begun at one week and was well advanced by two weeks so that the cortex of the graft near its union with the ilium was pitted by numerous small lacunas. These lacunas often had a scalloped outline and contained one or more osteoclasts. The cells seemed to arise from the ilium and to wander out along the surface of the graft. They also invaded the marrow canal of the rib graft along with connective tissue and blood vessels, and in the older specimens the cortex of the graft was in process of resorption on both its inner and its outer surface. In the eight and nineteen week specimens this resorption had progressed to such a degree that in some areas the graft was honeycombed in appearance.

In the earlier specimens the absorption of the graft was more evident on its convex (outer) surface and the opposite was true of the emptying of the lacunas in the bone. This surface was directly beneath and apposed to the muscles of the buttocks. Consequently, it was close to living tissues well supplied with blood, and we believe that this is responsible for the more marked osteoclastic activity and earlier resorption of the dead bone cells from the superficial lacunas which occurred in this area.

Delicate trabeculae of new bone were already present in the specimen removed one week after implantation of the graft in the ilium. These trabeculae arose from the cancellous bone of the ilium and extended to and in some areas were directly opposed and adherent to either the cortex or the end of the graft. In the two week specimen these trabeculae were more robust and numerous, and they were forming more appositional bone on the surface of the graft, but there was not yet solid bony union of the graft to either cortex of the ilium.

Fig. 3 (× 12).—Junction of cortical graft bone above with cortical host bone on the right after three weeks with pressure. A small amount of dense new bone has bridged the narrow gap. The rib is nonviable, as is the cortex of ilium adjacent to the drill hole. New bone inside the host is fairly dense. No appositional new bone is yet seen in this part of the bone graft. Note areas of osteoclasis inside and at edge of the graft.

At the pressure areas where the cortex of the graft was apposed to and pressed against the margin of the freshly cut hole in the cortex of the ilium we found two apparently dead bone surfaces in contact. The lacunas were empty, and there was a small amount of debris in the narrow space between the two bones, but there were no living cells or other signs of vitality and this condition also involved the acute angle between the rib and the outer cortex of the ilium while on the opposite side at the obtuse angle there was considerable new bone.

In the specimen removed three weeks after the operation these conditions are present at one point where the graft is in contact with the cortex of the ilium, but at another point the spaces between the acellular surfaces are a little wider, and here the new bone from the host has invaded and filled the space and firmly united the two apparently dead surfaces (fig. 3). In the older specimens this union became progressively more firm and the layer of new appositional bone on the outer surface

of the graft was more complete (fig. 4). Likewise the marrow canal was invaded by connective tissue, and trabeculae of new bone, as shown in figure 5. In most of the longer experiments a layer of appositional new bone was laid down on the inner surface of the cortex of the graft, so that we had the acellular remains of the cortex with a layer of living bone on either side (fig. 6). In some instances the marrow canals in the grafts were blocked near the end by fibrous connective tissue.

Fig. 4 (× 5).—Pressure side after six weeks. This section of the pressure side shows firm union of the rib to the host, and there is considerable apposition of new bone in the graft. At the acute angle, as shown by the arrow, cortex is united to cortex.

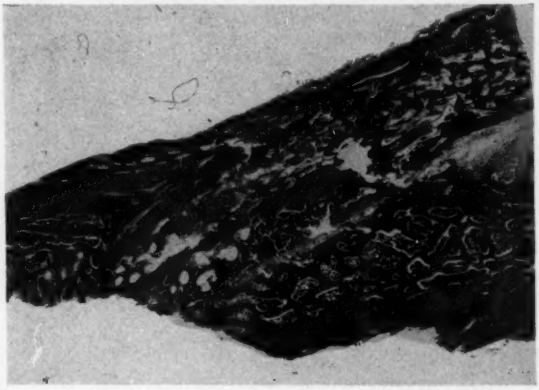

Fig. 5 (× 5).—Pressure side at eight weeks shows firm bony union of rib (above) to host on right. The rib has to a large extent been replaced by new bone, and marrow cells are present in the base of the rib.

Just as the acellular cortex of the graft is surrounded by two layers of living bone, so is the acellular zone in the cortex of the ilium around the drill hole surrounded by living bone as appositional new bone is laid down on its surface between it and the graft. This acellular zone can still be identified in the specimen removed 19 weeks after the operation but is much less prominent than in the earlier cases.

Nonpressure Side: On this side one end of the rib was inserted loosely in the relatively large drill hole and the other end was placed in the relatively wide groove in the ilium. Consequently, the spaces between the graft and the host bone were usually wider than on the pressure side. The extra space between the two bones

Fig. 6 (× 100).—This high power view shows the formation of appositional new bone above the surface of the apparently dead rib graft below at four weeks.

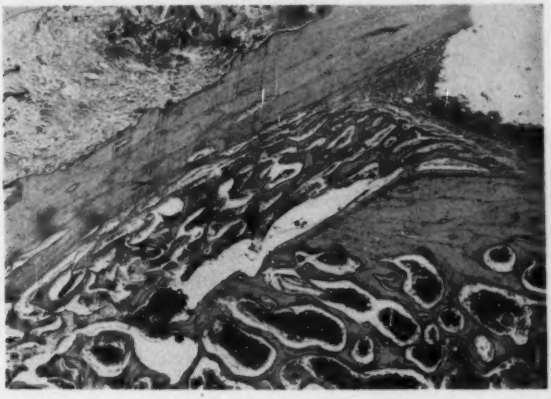

Fig. 7 (× 12).—Right side, without pressure, at three weeks. Although this rib was well inserted, as might be expected, apposition of the graft to the ilium is not as good as in figure 3. The space between is filled with new bone which is of necessity more abundant but less dense than that in figure 3. Fibrosis inside the rib is marked, as is osteoclasis, particularly inside this rib graft. The edge of the drill hole in the cortex of the ilium is sealed by a layer of appositional new bone.

necessitated a wider bridge of new bone between them in order to accomplish union, but we were not able to see that this caused an appreciable delay in the union of the two.

Here, as on the pressure side, delicate new bone trabeculae were present in the specimen examined one week after the insertion of the graft, and these appeared to

arise from the cancellous bone of the ilium and had reached the surface or end of the graft and appeared to be adherent to it. In the later specimens the new bone both from the cancellous portion and from the surface of the ilium had increased in amount and the trabeculae were thickened, so that by three weeks the graft and the host bone were bound firmly together and much of the surface of the graft was covered by appositional bone (fig. 7).

As would be expected, the amount of new bone appeared to be greater than on the pressure side because the spaces to be bridged were wider. In addition to the new bone trabeculae, the five and six week specimens exhibited small areas of hyaline cartilage in the new bone binding the graft to the ilium at the front. This cartilage resembled that seen in ordinary callus formed in the process of union of a fracture. No cartilage callus was seen in any of the specimens from the pressure side. In other respects the process of union between the graft and the host bone on the pressure side differed only in minor details, which could be accounted for by

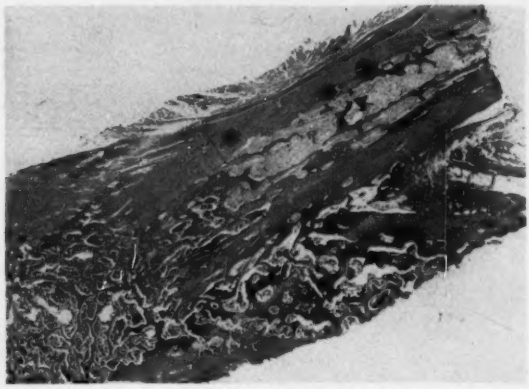

Fig. 8 (× 5).—Nonpressure side at eight weeks. As in figure 6, the graft is firmly united. Replacement of the rib by new bone is not as extensive as on the pressure side. The graft is filled with fibrous tissue away from the host.

variations in the orientation of the blocks and the areas from which the sections were made.

The changes in the rib graft and in the zone of cortical bone around the margin of the drill hole in the ilium were practically the same as those which occurred on the pressure side (fig. 8).

COMMENT

In the experiments here recorded an autogenous rib graft became united to the host bone (ilium). This union was accomplished by new bone which grew out from the host bone and became apposed to the graft, and the new living bone appeared to fuse to the surface of the acellular graft. For this fusion no pressure or even contact was necessary. It was only necessary that the bones be not too far apart and that one of them be living. In all the experiments in which the graft was left in place three weeks or longer firm union occurred.

Where two avascular surfaces, such as the surface of the graft and the margin of the drill hole in the cortex of the ilium, were apposed, there was no early union

of these surfaces even though they were pressed firmly together. Such surfaces became united by appositional new bone which invaded the narrow space and fused with each avascular surface, thus fusing the two bones. This appositional new bone came from the host, and we noted no osteogenesis on the part of the graft. If the pressure maintained close approximation between two acellular surfaces and thus prevented or inhibited the ingrowth of the new bone, union of these two cortical surfaces was delayed.

If it is recalled that when a bone is broken or cut the cells in the lacunas adjacent to the surface of the break or cut die and their lacunas become empty so that a narrow zone on either side of such a break or cut resembles dead bone, then it is evident that such surfaces do not grow together but are fused by living bone which grows in between them and fuses itself to each acellular surface.

Our observations suggest that the beneficial effects of pressure on bone union are due to the more complete immobilization effected by the pressure rather than to the pressure itself. Where the immobilization is less complete the callus is more abundant and is more likely to contain cartilage, as occurred in our experiments on the nonpressure side. The more abundant callus is necessary to span the space between the fragments, and we believe that one reason for the presence of the cartilage is that cartilaginous callus tends to immobilize the fragments while bony union is progressing.

Our experiments further suggest that close juxtaposition of acellular bone surfaces is a more favorable situation for union than is actual contact. It thus appears that pressure would exert a more favorable influence on cancellous bone than it would on compact bone, because trabeculae interdigitate. We even suggest that it may be wise, when applying a cortical bone graft, not to strive for application to the host under positive pressure, as with screws, but to place the graft in contact only, as recommended by Phemister, leaving minimal gaps to be filled by appositional new bone.

SUMMARY AND CONCLUSIONS

If juxtaposition and relative immobilization are maintained, bones tend to unite whether or not their surfaces are pressed together. In our experiments pressure made little difference in the manner or rate of union. New bone which appeared early arose from cancellous bone inside the host to fuse the autogenous bone grafts to the iliac bone. The last area in which union occurred was the point of immediate contact of the cortices of the graft and host.

Necrosis indicated by empty lacunas occurred in the autogenous grafts and in the host bone, adjacent to the defects made for insertion of the grafts. The area of the bone graft closest to the buttock muscles showed empty lacunas later than other areas.

Absorption of the bone grafts and ingrowth of fibrous tissue, new blood vessels and new bone occurred simultaneously, beginning at the base of the bone grafts, inside the host, and proceeding upward. Presence or absence of pressure seemingly made little difference in these processes.

Minor variations in the amount and consistency of callus which appeared were felt to be due to a difference in gaps which had to be bridged on the two sides and to better fixation of the grafts on the pressure side. Cartilage was noted in several instances on the nonpressure side but not on the pressure side.

There was no evidence that the bone grafts retained any viability or that any new bone arose from them.

ABSTRACT OF DISCUSSION

Dr. Leroy C. Abbott, San Francisco: In 1925, at the Shriner's Hospital for Crippled Children in St. Louis, we performed our first operation (slide) for arthrodesis of the hip by the so-called wide abduction method. Massive destruction of the head and neck of the femur had resulted from tuberculosis. In this case fusion occurred, as it did in a high percentage of patients operated on in a similar manner during the next five years. The principle of this operation was the wide apposition of cancellous bone surfaces of the ilium and the great trochanter, with pressure and fixation. Dr. Albert Key applied this same principle in excision of the knee, with pressure and fixation by means of pins and turnbuckles.

The papers presented today represent the efforts of two groups of investigators to settle the arguments for or against the beneficial influence of compression and contact on osteogenesis. The conclusions of these two groups are diametrically opposite. One group contends that compression is necessary and a useful physical influence, while the other group is convinced that compression is neither essential nor, in certain cases, desirable. Might I suggest that perhaps the bones which were used may be held accountable, in some measure at least, for these divergent opinions? Furthermore, a critical analysis suggests that there is no absolute certainty that compression was maintained in either group of experiments, except during the first few days after operation. It may well be that the final decision on the effect of compression will await a group of scientific investigators, which will include the engineer. He will insist on the use of strain gages to ascertain whether it is impression only or whether compression is actually maintained during the entire healing process.

I am very much pleased at the opportunity to discuss these fine papers. They provide stimulus to further thought and experiment on the entire subject of the healing of bone.

Dr. Arch F. O'Donoghue, Sioux City, Iowa: We should all be grateful to both the investigators here for trying to throw some light on a subject which has been discussed by orthopedic men for at least 25 or 30 years. It has been recognized by most surgeons for years that bones seem to heal better when contact between the fractured surfaces or the bone grafts was applied in such a manner that there would be definite positive pressure between the ends of the fractured bones or between the grafts and their hosts.

The idea that positive pressure was helpful in treating fresh transcervical fractures of the hip by use of a bone graft was presented by us three years ago; the grafts being triangular in shape and cut slightly larger than the hole which was drilled across the fracture line makes positive pressure between the graft and the host, further aided by being held by screws in which the threaded portion is larger than the shank, so that compressive force is exerted against the fracture as the screws are turned home.

[Slide] As you know, Key in 1932 described a method of speeding up knee fusions by the use of two pins, one in the femur and one in the tibia, with rubber bands between them to create positive pressure, which he found useful and which has since been somewhat modified by Charnley, who has become enthusiastic about obtaining fusion by this means.

We believe that Dr. Eggers has shown this well with his experiment on membranous bone and with the contact splint which he has devised. I do not believe that Dr. Ford's work has entirely disproved it, either, because the pressure factor is a marked variant in the work done by Dr. Ford.

It remains for further experimental work to be done to discover how much or how little positive pressure is necessary to stimulate osteogenesis to the optimum amount. We all know that too much pressure is likely to cause necrosis. Possibly experiments of the type that we have now started, which will take some years to complete, may be helpful. We are attempting to treat some fractures of the tibia and fibula by using positive pressure calibrated against two small spring scales to see if any conclusion can be reached about optimum pressure.

Dr. Lee T. Ford, St. Louis: We have another experimental problem which when completed may give some additional information on this interesting matter of the effect of pressure on the healing of bone.

Dr. Abbott mentioned that the arthrodesis of the knee by the method of Key was by positive pressure. This is true. However, this positive pressure involves cancellous bone and care must be taken not to apply too much pressure.

In reviewing the experimental work on the parietal bone of rats as done by Dr. Eggers and others, we felt that in the control bone in which no pressure was applied there was obviously a larger gap which had to be filled with new bone. On the pressure side of the experiment, however, bone was in actual contact, in many spaces there being no gap to be filled. In other areas in which contact was present and excessive pressure was applied definite necrosis of bone was present in several of their sections.

One reason we performed these experiments using bone grafts was that we were interested in knowing how bone other than that of the skull of the rat would behave when subjected to pressure.

Dr. George W. N. Eggers, Galveston, Texas: In regard to the continuous compression, we have endeavored to do that the best way we know by using split rubber bands, with the idea that they would continue the pressure throughout the experiment.

I spoke to Dr. Key about the work in regard to the ilium at one time. I did not have the privilege of seeing or hearing the paper until now. I shall just call your attention to one or two analytical points in regard to it. One is that they are using a graft where we used a living flap. The other is that they covered the flaps with the musculature of the ilium. As soon as you cover the graft with the musculature of the ilium, you have thereby created an active muscular area which will cause certain pressures on the graft which is placed on the ilium. Their control on nonpressure rib grafts is actually under the pressure of the iliac muscles, as I understand it.

SLUDGED BLOOD

A Critique

HAROLD LAUFMAN, M.D., Ph.D.
CHICAGO

IT IS NOW eight years since Knisely and his associates first reported their observations on the curious phenomenon of red cell agglutination within vascular walls. To this phenomenon they applied the term "sludge." A great deal of earnest and interested work has been done, and many articles on the subject have been published showing the presence of sludged blood in conjunction with nearly all pathologic conditions of the body. It has been found coincident with disease, shock and trauma of all sorts; its ubiquity challenged investigators to perform the difficult tasks of accounting for its presence and determining its significance. By 1947 the concept of sludge, by virtue of the widest implications given it, had become the nexus of a whole system of thinking about disease. It had become somehow identified as the cause of specific pathologic findings or of complications in conditions which it accompanied.

Sludge, for example, is supposed to play a major role in mental disease ("It is now obvious that several groups of psychiatric patients now need to be studied to determine the role which sludge is playing or has played in their pathologic physiology"[1]; in senility ". . . It becomes obvious that we now need to begin to determine carefully how all the damages done to the body by sludges can summate as parts of the aging processes"[1]), and in postburn shock ("Sludging of the blood following burns now seems to be a mechanism sufficient to initiate shock . . ."[2]).

If sludge plays a crucial role in so many major pathologic states, it could almost be thought of as a "total disease," a counterpart in the field of pathology to the idea of a total medicine, or panacea, in the field of therapy. Such wide claims demand careful examination.

In none of the quotations just given appears a direct statement that sludge is the prime causal factor of pathologic processes, but the contents out of which such statements come provide an elaborate architectonic of reasoning which gives so overwhelming an impression of the importance of sludge that we tend to believe we know more about it than we actually do.

Knisely says:

> The observations, experiments and deductions outlined above are evidence that the sludges provide a common, easily understandable set of factors whereby many diseases can and do damage the bodies of animals and man.[1]

Read before the Chicago Surgical Society, Nov. 3, 1950.

From the Department of Surgery, Northwestern University Medical School.

1. Knisely, M. H.; Bloch, E. H.; Eliot, T. S., and Warner, L.: Sludged Blood, Science **106**:431, 1947.

2. Brooks, F.; Dragstedt, L. R.; Warner, L., and Knisely, M. H.: Sludged Blood Following Severe Thermal Burns, Arch. Surg. **61**:387 (Sept.) 1950.

Thus, the concept of sludge within this system of thinking provides an open sesame to the understanding of an almost endless series of pathologic processes. We need now to ask for the established facts on which this inclusive concept has been based.

The following discussion represents a painstaking analysis of the literature on the subject of sludged blood and an account of some observations made by my colleagues and me at Northwestern University in the attempt to discover what facts we could about sludge and to arrive, if possible, at some ideas about its practical significance. When the published material was accumulated and our own observations noted,[3] I became aware of three logical difficulties in the attempt to evaluate the potential meaning of the sludge phenomenon. First, observers are unable to agree on what they observe; second, interpretations of observations rather than the observations themselves are used as the premises of argument, and, third, deductions are made on the basis of inadequately established premises. This report, therefore, assumes the character of a critique.

In examining the first difficulty, that of opposing observations, I must recount our experiences. For the past three years we have made many observations on animals and patients [4] under various conditions about the phenomenon of sludge. In a study of the reactions of small blood vessels of the mesentery and their responses to various types of vascular occlusions we had occasion to observe the nature of the blood within the vessels.[5] By producing stagnant anoxia in the mesenteric vascular tree we were able to produce intravascular agglutination at will. This fascinating phenomenon arrested our attention, and on the conclusion of our other experiments [6] we continued to study the general problem of intravascular agglutination in both animals and patients.

Knisely and his co-workers have stated, "completely unagglutinated blood has been found strictly in healthy animals and men" and "no severely ill person has yet been seen who did not have intravascular agglutination of the blood and visibly pathological walls." [7] On the other hand, several other groups of investigators,[8]

3. Laufman, H.; Gobrewski, R.; Treger, N.; Method, H., and Tanturi, C. A.: The Significance of the Blood "Sludge" Phenomenon, Quart. Bull., Northwestern Univ. M. School **24**:257, 1950.

4. Laufman, H.; Martin, W. B., and Tanturi, C. A.: Effect of Heparin and Dicoumarol on Sludge Formation, Science **108**: 283, 1948. Laufman and others.[3]

5. Laufman, H.; Martin, W. B., and Tuell, S. W.: The Pattern of Vasospasm Following Acute Arterial and Venous Occlusions: Micrometric Study, Surg., Gynec. & Obst. **87**:641, 1948.

6. Martin, W. B.; Laufman, H., and Tuell, S. W.: Rationale of Therapy in Acute Vascular Occlusions Based upon Micrometric Observations, Ann. Surg. **129**:476, 1949. Footnotes 4 and 5.

7. Knisely, M. H.; Eliot, T. S., and Bloch, E. H.: Sludged Blood in Traumatic Shock: Microscopic Observations of Precipitation and Agglutination of Blood Flowing Through Vessels in Crushed Tissues, Arch. Surg. **51**:220 (Nov.-Dec.) 1945.

8. Hirschboeck, J. S., and Woo, M.: A Clinical Evaluation of the Blood "Sludge" Phenomenon, Am. J. M. Sc. **219**:538, 1950. Lack, A.; Adolph, W.; Ralston, W.; Leiby, G.; Winsor, T., and Griffith, G.: Biomicroscopy of Conjunctival Vessels in Hypertension: A Capillary "Hypertension Pattern" and the Occurrence of Intravascular Clumping (Sludged Blood) Are Described, Am. Heart J. **38**:654, 1949. Bellis, C. J., and Snow, H. L.: Sludged Blood: The Electrokinetic Factors Involved, Ann. West. Med. & Surg. **4**:223, 1950.

notably Robertson, Wolf and Wolff,[9] have made the following conclusions after an intensive investigation:

> On the basis of day to day studies of normal subjects and patients with a variety of disease states and of observations with vasomotor drugs . . . it is evident that widespread sludging in the conjunctival vessels is compatible with good health and well being.

From our own more limited observations [8] we were faced with one outstanding fact, namely, that our diagnostic means were unable to detect any observable disease process in a series of young patients (under 30), let alone a group of older patients who possessed no acute, chronic, severe or mild disease but whose conjunctival vessels carried heavily sludged blood. Also, we observed an elderly hypertensive patient who had tertiary syphilis and whose vessels showed no sludged blood. It is possible that sludge is such a sensitive reflection of subclinical disease and that the detection of the latter defies identification by ordinary clinical means. It is also possible that low grade, indiscernible, nonsymptomatic afflictions, such as some stages of sinusitis, exist in Chicago or in New York, where Robertson's group worked, and not in Tennessee, where Bloch [10] made his observations. However, the discrepancy in observational conclusions by different groups of dependable and experienced investigators is confusing.

Another example of opposing observations concerns what Knisely has termed a "key fact," which is that "at all times the blood coming down the arterioles of an uninjured conjunctiva is a statistical valid sample of all the flow of arterial blood in the body." [7] Heimbecker and Bigelow [11] of Toronto do not concur in this observation. Knisely bases his statement on the fact that he has opened many animals and studied the blood passing through many different organs. However, not anywhere in his reports have we been able to find that these observations were ever made simultaneously on the different organs in the same animals. Heimbecker and Bigelow produced shock in several ways in animals and found that the degree of sludging in the conjunctiva and nictitating membrane was invariably more marked than that observed in the omentum and mesentery. The latter showed stasis and vasoconstriction only with the animal in deep shock following severe trauma. These workers used this observation to support the evidence that vasoconstriction affects cutaneous vessels much earlier than visceral vessels. Several of Knisely's own observations would seem to reject the statement expressed in his key fact. In his work on traumatic shock [7] he described three main zones in the area of trauma to striated muscle. The innermost zone contained vessels in which there was no flow. The intermedial zone contained vessels with heavily sludged blood. The outer zone contained vessels without sludge. If three zones practically within the same microscopic field vary to this extent the character of the blood flowing throughout the entire body will probably not be uniform. All observers who have studied sludge in conjunctival vessels have noted that while some vessels in a given microscopic field are heavily sludged the flow through neighboring vessels is apparently

9. Robertson, H. S.; Wolf, S., and Wolff, H. G.: Blood "Sludge" Phenomenon in Human Subjects: Notes on Its Significance and on the Effects of Vasomotor Drugs, Am. J. M. Sc. **219**:534, 1950.

10. Knisely, M. H., and Bloch, E. H.: Intravascular Agglutination of Erythrocytes in Disease, with Cinema Demonstration, Proc. Inst. Med. Chicago **15**:281, 1945.

11. Heimbecker, R. O., and Bigelow, W. G.: Intravascular Agglutination of Erythrocytes and Traumatic Shock, Surgery **28**:461, 1950.

normal. There are many other examples of opposing observations in the literature on sludge, for which the above examples will suffice.

A second difficulty which we found was that an investigator used interpretations of observations rather than the observations themselves as the premise of argument and furthermore that deductions were made on the basis of inadequately established premises. Both of these examples of illogic must of necessity be discussed together, since in many instances within one sentence there is such a tight intertwining of fact and fancy that extrication of one from the other would be too difficult for anyone but a professional logician. I should like to quote a few of these passages and comment on them from a practical perspective. Rather than risk the possibility of quoting out of context I shall quote an entire paragraph from one article.

> One young woman referred to us from a psychiatric division because she had a slightly elevated red cell sedimentation rate in addition to her "functional" psychological disturbances had 8 small permanent plugs in the terminal arterioles of the bulbar conjunctiva of one side of one eye. They were in different stages of the familiar hemoglobin chemical disintegration color series. Every once in a while a slightly smaller mass came along, temporarily plugged a vessel, and passed on again. Two weeks later the patient had three more similar permanent embolae of terminal conjunctival arterioles. From the branching pattern of the aorta and the great arteries to the head, and the fact that the blood going to the eye comes directly from these, one cannot doubt that this woman's whole central nervous system was slowly showered with permanent plugs, each of which destroyed a small volume of irreplaceable nerve cells. When one considers the parallelism between the known effects on normal persons of breathing slowly decreasing concentrations of oxygen (cerebral effects of anoxia), the slightly to greatly increased irritability, the euphoric tendency to laugh uproariously at meaningless trivia, the dull-witted phrases, the compulsive behavior at times, and the comatose condition as the anoxia approaches the lethal stage, and similar phases of some of the symptom complexes studied in mental hospitals, it is obvious that several groups of psychiatric patients now need to be studied to determine the role which sludge is playing or has played in their pathologic physiology. Osler himself pointed out that psychic disturbances can and do follow infectious diseases.[1]

In this statement there are two pertinent facts: (1) sludge occurred in one part of one eye and (2) blood going to the eye comes directly from a branching pattern of aorta and great arteries to the head. It is difficult to see how these two facts lead to a conclusion that the patient's entire nervous system was slowly showered with permanent plugs. Also we do not find any support among the facts known on the pathology of the brain for the supposition that these hypothetical permanent plugs can destroy a small volume of irreplaceable nerve cells. I mention this not as positive evidence for anything but negatively, to demonstrate that not only is there no evidence to support the quotation but also that the known evidence renders it improbable. One must consider, however, the possibility that physiochemical changes within brain cells need not be demonstrable pathologically. The positiveness of the quotation appears unwarranted at this time. The last sentence of the paragraph regarding the fact that Osler pointed out that psychic disturbances can and do follow infectious diseases hardly bears analysis. We are to deduce, because a great authority noted that psychic disturbances follow infections and because we know that sludge follows infections, that therefore sludge causes psychic disturbances.

Another quotation is as follows:

> When one considers the numbers of already observed pathologic conditions during which a sludge was present, the fact that many sludges could be expected to do at least small amounts

of permanent damage to the body, the fact that these damages must be cumulative over a long period, and the pitiful mental incompetence of the prematurely senile and of many aged persons, it becomes obvious that we now need to begin to determine carefully how all the damages done to the body by sludges can summate as parts of the aging process.[1]

It has not been established as a fact that "many sludges could be expected to do small amounts of permanent damage," nor has it been established as a fact that "these damages may be cumulative over a long period." That senile incompetence is pitiful is true, but it is irrelevant here. It would appear premature to determine *how* sludge damages the body when it is not yet established *whether* sludge damages the body. Sludge may well do damage, but evidence to show that it does has not yet appeared. Therefore, while the suggestion that further studies be made is technically only a suggestion, the reasoning out of which it grew is so involved and the suggestion so authoritative that the gaps in logic can easily be overlooked.

The following statement is from the same article:

In which different and overlapping combinations can the anatomical and physiological decrements caused by sludges, and readjustments to these, summate over periods of years? How rapidly can they add up over short periods? How do these factors cumulate along with other nonsludge factors in the various aging processes?[1]

These questions are leading. They assume that it has been established that the cumulative effects of sludge are contributory in the aging process. This has not been established.

Brooks and his co-workers [2] burned a series of laboratory animals and observed that sludge appeared shortly afterward. If the sludge became thicker, they reasoned that this thick circulating blood must have an anoxic effect on the tissues of the body. They therefore arrived at the following statement:

Sludging of the blood following burns now seems to be a mechanism sufficient to initiate shock, but whether it is the only mechanism present after burn which is capable of initiating a shock state can be determined only by finding whether or not factors sufficient to produce a shock state occur in the absence of this sludging.

Again no direct evidence in this work established sludge as one of many factors capable of initiating shock, let alone the only mechanism. Our relevant information from Brooks's report is limited to the observation that sludge follows burns, a fact which by itself does not justify a hypothesis that sludge is the cause of shock. Sludge occurs in the presence of any severe trauma. Such trauma may be followed by shock. Burns, then, may lead to shock, and burn shock, like other kinds is accompanied with or may follow the appearance of sludge. But temporal priority does not infallibly establish causal relationship.

If early postburn sludge causes shock, why does not late postburn sludge cause shock? There are thousands of persons going about their daily businesses with heavy sludge in their vessels. Why do they not go into shock? Where and what is the delimiting factor which allows sludge to cause shock in some circumstances and not in others? Similar questions of a critical nature can be applied to the suggestion made in this same article that sludge is a cause of such things as postburn toxicity or postburn anemia.

We know of no evidence indicating that sludge itself (not other factors of trauma) "initiates" shock. Even if we could establish that it does, no additional proof would be obtained by "finding whether or not factors sufficient to produce a

shock state occur in the absence of sludging." If it could be demonstrated that shock can occur in the absence of sludging, we should know something more about shock but nothing more about the effects of sludge. If, on the other hand, no such factors are found, we should still have established only that sludge, among other things, accompanies shock and not that sludge is the cause of shock.

Heimbecker and Bigelow [11] have published a series of experiments in which they showed that a state of clinical shock can occur in the absence of sludge. Clinical shock in the absence of sludge was produced by hemoconcentration, by graded hemorrhage and by injections of histamine. No red cell clumping was observed in any of these shock states. Progressive slowing of the rate of flow occurred, but no vascular stasis had appeared until the shock became very severe. These authors find it difficult to judge to what degree the reduced rate of flow and capillary stasis in traumatic shock is due to red cell clumps.

Further, they were able to present convincing evidence that generalized intravascular clumping occurs following light trauma without shock. Why did not this intravascular clumping result in a state of shock as it allegedly did in the heavier types of trauma with shock? It is interesting that the degree of sludging bears no relationship to the degree of trauma. This last bit of information would appear further to negate the importance of sludge as a factor in the production of shock.

Regarding the question as to whether the abnormal flow in the vascular bed in traumatic shock is due entirely to the effects of intravascular agglutination, Heimbecker and Bigelow showed that the presence of agglutinated red cells alone produced only a slight abnormality in the flow in the microscopic vascular bed; but when the blood pressure dropped, when peripheral vasoconstriction occurred and hemoconcentration was superimposed, the flow became much more abnormal. Correction of the latter factor by infusions of plasma and saline corrected the shock state and reduced the degree of vascular stasis remarkably. This treatment also appeared to reduce the degree of erythrocyte agglutination, but the latter was still present to a certain degree even after the shock state was repaired. Heimbecker and Bigelow point out that in conducting studies on the living vascular bed one must be careful to recognize that a slow flow can be obtained by hemoconcentration and low blood pressure, in the presence of intravascular agglutination.

A wide variety of speculative concepts has been published on the significance of sludge in pathologic conditions. Already mentioned are such diverse conditions as dementia praecox, senile dementia, the aging process itself, postburn shock, postburn toxicity and postburn anemia. In addition to these, one is led to infer that sludge may play an important role in necrosis of the liver following burns,[2] postoperative pulmonary embolism,[1] edema of the extremities,[1] coma,[1] arteriosclerosis [1] and several other phenomena as yet poorly understood.

It is possible that sludging causes these diverse conditions, but there is as yet no valid evidence to support the thesis. In a recent article [3] we suggested some equally undemonstrated and equally possible lines of thought on the subject. The fact remains that sludge is concomitant with a wide variety of disease states, that its presence and the nature of its relationship to other phenomena and processes are as yet unexplained and that all of us are eager to hear of any new facts which might enable us to form some reasonable hypotheses on which to predicate future work.

Microscopic observations are not sufficient to substantiate such conjectures as have been quoted here. Determination of the effects of sludge on body processes involves so many associated phenomena that bona fide evidence would necessarily be the product of work in the fields of physiology, physiological chemistry, physical chemistry and allied sciences. For such an investigation to be fruitful, a large part of it would have to concentrate on the causes of sludge, not so much in terms of what clinically recognizable disease states might cause it, but more especially in terms of alterations in the colloid chemistry of blood proteins induced by physical, chemical or immunologic effectors. The eventual value of the results of such experimentation to the practicing physician or surgeon cannot be predicted in advance.

Therefore, until factual information is available, favorite hypotheses must be regarded as hypotheses and not as conclusions. Premature and oversimplified explanations of so complicated a phenomenon can lead only to further confusion.

STUDIES ON 5-AMINOACRIDINE

I. In Vitro Bacteriologic Evaluation on Peritoneal Exudate from Induced Fulminating Peritonitis

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THE ACRIDINE group of antiseptics were used by surgical teams during part of the first World War and sporadically thereafter. During World War II, in an effort to find an effective agent in cases of resistance to penicillin and sulfonamides, the interest in the acridines was revived and remarkable success was reported with certain of the derivatives by British and Australian investigators.[1] Added stimulus has been supplied by the synthesis in recent years by Adrien Albert and his colleagues [2] of equally effective but less toxic derivatives, notably 2-7 diaminoacridine hydrochloride and 5-aminoacridine hydrochloride.

In 1945, one of us (H.R.H.) began using 5-aminoacridine hydrochloride in solution locally in infected wounds, in contaminated perineal wounds following abdominoperineal resection and in compound fractures with sepsis encountered in a civilian hospital. Sulfonamides, penicillin and supportive measures had been fully employed without appreciable effect on the local condition prior to the use of 5-aminoacridine. Although the series was small, the results were sufficiently gratifying so that experiments were undertaken to determine the feasibility of administering the acridines systemically and intraperitoneally.

In view of the effective inhibiting power of 5-aminoacridine in high dilutions against strains of Clostridium welchii, Escherichia coli, Staphylococcus aureus, and certain strains of streptococci,[3] it was hoped that a useful adjunct in the treatment of peritonitis might be found. Because of its low toxicity on local appli-

Aided by a grant from the National Drug Company, Philadelphia.

The acridine drugs were kindly supplied to us by the National Drug Company.

From the Harrison Department of Surgical Research Schools of Medicine, University of Pennsylvania and the Graduate Hospital.

1. Mitchell, G. A. G., and Buttle, G. A. H.: Proflavine Powder in Wound Therapy, Lancet **2**:416, 1942; Diflavine in Wound Therapy, Lancet **2**:287, 1943. Poate, H. R. G.: Acridines in Septic Wounds: Use of 5-Aminoacridine, Lancet **2**:238, 1944.

2. Albert, A.; Dyer, F. J., and Linnell, W. H.: Chemotherapeutic Studies in the Acridine Series: IV. The Relations Between Structure and Toxicity, Quart. J. Pharm. & Pharmacol. **10**:649, 1937. Albert, A.; Goldacre, R., and Rubbo, S. D.: Further Correlation of Physical and Biological Properties in Acridine Series, Nature, London **147**:709, 1941.

(Footnotes continued on next page)

cation and its high bacteriostatic properties 5-aminoacridine hydrochloride was the drug chosen for this study and was the one used throughout the course of the experiments.

For our purposes, the investigation of the drug was developed along three lines: (1) a study of the pharmacology and toxicology of 5-aminoacridine following parenteral administration into normal animals; (2) the in vitro effectiveness of 5-aminoacridine alone and in comparison with other antibiotics on peritoneal exudate from an induced fulminating peritonitis; (3) parenteral administration of the drug to dogs having fulminating peritonitis. The first and third of these lines of investigation are considered in a separate communication. This report is concerned with the in vitro bacteriologic evaluation of 5-aminoacridine on dog peritoneal exudate.

It was felt that a comparative study of 5-aminoacridine with streptomycin, penicillin and sulfadiazine, alone and in combination with each of the three drugs, would provide useful information on the in vitro activity of the drug. This study would also perhaps indicate possible synergistic or additive effects. Likewise, in order to determine any increased activity of the drug as a result of smaller initial inoculums, a parallel series of determinations was run in which the exudate was diluted 1 to 10.

The peritoneal exudate was obtained in the following manner: Fulminating peritonitis was created in dogs by ligating and slitting the appendix after the method of Zintel, Wiley, Nichols and Rhoads,[4] as recommended by Harvey, Meleney and Rennie.[5] The exudate was collected immediately on the death of the animal. The organisms present in peritoneal exudate from appendical peritonitis have been discussed at length by Meleney and his co-workers,[6] and our findings are identical with theirs. A total of five exudates were studied. The determinations were started within one to three hours after withdrawal, the material being kept in the incubator at 37 C. in the interim. Since it is known that

3. Rubbo, S. D.; Albert, A., and Maxwell, M.: Influence of Chemical Constitution on Antiseptic Activity; Study of Mono-Aminoacridines, Brit. J. Exper. Path. **23**:69, 1942. Albert, A.; Rubbo, S. D.; Goldacre, R. J., and Davey, M. E.: Influence of Chemical Constitution on Antibacterial Activity: General Survey of Acridine Series, Brit. J. Exper. Path. **26**:160, 1945. Ungar, J., and Robinson, F. A.: Investigation of Antibacterial and Toxic Action of Certain Acridine Derivatives, J. Pharmacol. & Exper. Therap. **80**:217, 1944; Aminoacridine Antiseptics: Comparison of 2:7 Diaminoacridine, 5-Aminoacridine and Proflavine, Lancet **2**:285, 1943. Browning, C. H.: Present Status of Aminoacridine Compounds (Flavines) as Surface Antiseptics, Brit. M. J. **1**:341, 1943.

4. Zintel, H. A.; Wiley, M.; Nichols, A., and Rhoads, J. E.: Use of Streptomycin in Surgical Patients, Surgery **21**:175, 1947.

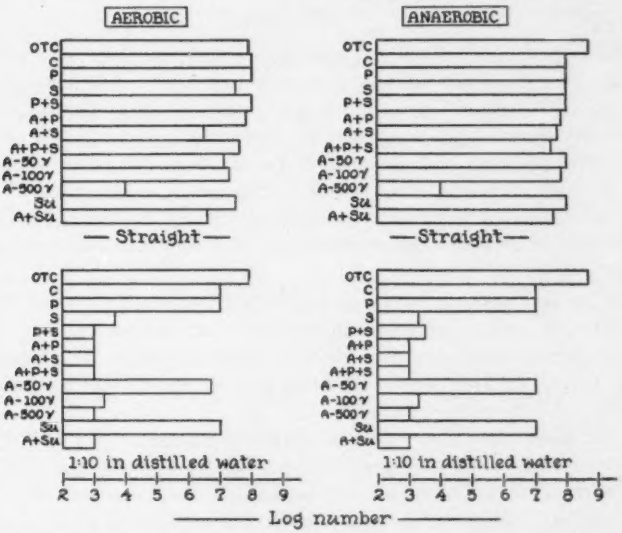
5. Harvey, H. D.; Meleney, F. L., and Rennie, J. W. R.: Peritonitis: Studies in Peritoneal Protection with Particular Reference to Action of Sulfonamide Drugs in Experimental Peritonitis, Surgery **11**:244, 1942.

6. Meleney, F. L.; Harvey, H. D., and Jern, H. Z.: Peritonitis: Correlation of Bacteriology of Peritoneal Exudate and Clinical Course of Disease in 106 Cases of Peritonitis, Arch. Surg. **22**:1 (Jan.) 1931. Meleney, F. L.; Olpp, J.; Harvey, H. D., and Jern, H. Z.: Peritonitis: Synergism of Bacteria Commonly Found in Peritoneal Exudates, Arch. Surg. **25**:709 (Oct.) 1932.

anaerobic micro-organisms play an important role in peritonitis, both aerobic and anaerobic determinations were made.

PROCEDURE

As soon as possible after obtaining the exudate, an initial aerobic and anaerobic total viable bacterial count was started. This will be referred to hereafter as 0 time count (OTC). Five-tenths milliliter of exudate was diluted in saline in tenfold serial dilutions up to 100,000,000. One milliliter of each dilution was then pipetted into duplicate Petri plates and approximately 20 ml. of 5 per cent horse blood extract agar, p_H 7.2, poured into each plate and thoroughly mixed. One series was incubated aerobically and the other anaerobically for 48 hours.



Graph of the logs of the total aerobic and anaerobic counts of viable bacteria in exudate number two, straight and diluted 1 : 10 in distilled water after exposure to the various antibacterial agents or combinations of these agents for 24 hours. See text for symbols and concentrations.

One series of 12 tubes containing 5 ml. each of straight exudate and another series with the exudate diluted 1 : 10 with distilled water were prepared. To the first tubes in each series 1 ml. of distilled water was added as a control, hereafter referred to as control (C). To the remaining tubes of each series was added 1 ml. of the appropriate drug in distilled water. Each milliliter of drug or combination of drugs contained five times the desired final concentration in the exudate with the exception of 500 gamma of acridine where the approximate maximum solubility in distilled water is 1 mg. per milliliter. This necessitated adding 2.5 ml. of a 1 mg. per milliliter solution to the 5 ml. of exudate. The tubes were thoroughly mixed and incubated at 37 C. for six hours.

The following list gives the various antibacterial agents or combination of agents, their final concentration per milliliter of exudate and their corresponding symbols to be referred to in this report.

OTC = Zero time control
C = Control for distilled water
P = Penicillin 1 unit per ml.
S = Streptomycin 10 units per ml.
P+S = Streptomycin 10 units per ml. and penicillin 1 unit per ml.
A+P = Acridine 100 γ per ml. and penicillin 1 unit per ml.
A+S = Acridine 100 γ per ml. and streptomycin 10 units per ml.
A+P+S = Acridine 100 γ per ml., streptomycin 10 units per ml. and penicillin 1 unit per ml.
A-50 = Acridine 50 γ per ml.
A-100 = Acridine 100 γ per ml.
A-500 = Acridine 500 γ per ml.
Su = Sulfadiazine 10 mg. per 100 ml.
A+Su = Sulfadiazine 10 mg. per 100 ml. and acridine 100 γ per ml.

At the end of the six hour exposure tenfold serial dilutions were made from each tube. Since only two dilutions were to be plated out it was necessary, in the case of the six hour exposure series, to plate out two widely spaced dilutions to insure counts at both upper and lower extremes. In most cases this resulted in dilutions of ten thousand and one million. For this reason, some of the end points in the six hour exposures were missed. This was especially true of the first exudate, which had a much lower count than anticipated. However, this presented no problem in the 24 hour exposure counts, because there was available a tentative zero time control.

Thus, for each drug or combination of drugs, two dilutions were plated out in duplicate (for aerobic and anaerobic incubation) at six hour and 24 hour intervals. An identical series was run when the original exudate was diluted 1 : 10. Five per cent defibrinated (filtered through cotton) horse blood in extract agar, p_H 7.2, was used throughout the work.

All final counts were made after 48 hours' incubation at 37 C. Entire plate counts were made on those plates containing 500 or less colonies. Plates containing 500 to 1,000 colonies were estimated by counting a sector. These counts are recorded as approximations in the table, which gives the bacterial count in exudate number two after exposure to various bacterial agents or combinations of agents for six hours and 24 hours. Plates containing more than 1,000 colonies are indicated as greater than 1,000 times the highest dilution. Likewise, those plates having no colonies on the lowest dilution plate are indicated as having less than the lowest dilution number of colonies.

RESULTS AND COMMENT

All five exudates responded in a similar manner to the concentrations of the drugs used. The accompanying graph, the actual figures for which can be found in the table, is a representative picture of what occurred in all five exudates. Since the type and number of organisms varied from one exudate to another, slight differences in response to any one particular drug might be expected. This was especially true of streptomycin and penicillin; in one exudate the response would be better with streptomycin than with penicillin and in another exudate

the reverse would be true. In this respect it is interesting to note that in every case 100 gamma per milliliter of acridine was just as effective or more so than either streptomycin or penicillin and 500 gamma per milliliter of acridine was decidedly more so.

There appears to be no significant difference in response between the anaerobic and the aerobic series. It may be assumed that facultative anaerobes in the anaer-

Total Aerobic and Anaerobic Counts of Viable Bacteria in Exudate Number Two After Exposure to Various Antibacterial Agents or Combinations of These Agents for Six Hours and Twenty-Four Hours

Antibacterial Agents	Aerobic		Anaerobic	
	6 Hours	24 Hours	6 Hours	24 Hours
Straight Exudate Multiply Figures × 10^3				
Zero time control	.....	90,000	.....	465,000
Control for distilled water	97,000	>100,000	>1,000,000	>100,000
Penicillin 1 unit per ml.	108,000	>100,000	65,000	>100,000
Streptomycin 10 units per ml.	61,000	32,000	350,000	>100,000
Streptomycin 10 units per ml. and penicillin 1 unit per ml.	17,000	>100,000	36,000	>100,000
Acridine 100 γ per ml. and penicillin 1 unit per ml.	10,000	60,000*	7,000	80,000*
Acridine 100 γ per ml. and streptomycin 10 units per ml.	12,000	2,975	45,000	50,800
Acridine 100 γ per ml., streptomycin 10 units per ml. and penicillin 1 unit per ml.	10,000	39,200	2,000	29,000
Acridine 50 γ per ml.	33,000	13,700	280,000	>100,000
Acridine 100 γ per ml.	14,000	<18,500	55,000	60,000*
Acridine 500 γ per ml.	570	10	600	<10
Sulfadiazine 10 mg. per 100 ml.	240,000	30,800	>1,000,000	>100,000
Sulfadiazine 10 mg. per 100 ml. and acridine 100 γ per ml.	4,520	4,200	52,000	40,800
Exudate 1:10 Multiply Figures × 10^3				
Zero time control	.....	90,000	.....	465,000
Control for distilled water	41,800	>10,000	51,200	>10,000
Penicillin 1 unit per ml.	>100,000	>10,000	>100,000	>10,000
Streptomycin 10 units per ml.	500	5	1,800	2
Streptomycin 10 units per ml. and penicillin 1 unit per ml.	314	<1	700	3
Acridine 100 γ per ml. and penicillin 1 unit per ml.	95	<1	28	1
Acridine 100 γ per ml. and streptomycin 10 units per ml.	290	<1	95	1
Acridine 100 γ per ml., streptomycin 10 units per ml. and penicillin 1 unit per ml.	5	<1	3	1
Acridine 50 γ per ml.	1,700	5,200	3,000	>10,000
Acridine 100 γ per ml.	325	2	210	2
Acridine 500 γ per ml.	<1	<1	9,000	<1
Sulfadiazine 10 mg. per 100 cc.	8,100	>10,000	29,000	>10,000
Sulfadiazine 10 mg. per 100 cc. and acridine 100 γ per ml.	11	<1	16	<1

* An approximation where there were more than 500 colonies on the plate of highest dilution.
> More than 1,000 colonies on the plate of highest dilution.
< No colonies on plate of lowest dilution.

obic series responded in an identical manner as in the aerobic series and that any differences in the total number of organisms could be attributed to the strict anaerobes.

On dilution of the original exudate 1 : 10 with distilled water, the response was much superior, especially when the acridine was involved. There are at least two explanations for this increased activity. Either inactivating or neutralizing substances in the exudate have been diluted and/or the original inoculum has been reduced tenfold. The presence of such substances as penicillinase, glucose

and adenylic acid in dog peritoneal exudate has been shown by many workers, and undoubtedly these were diluted beyond their maximum effectiveness. That reduction of the original inoculum played an important role is shown by the fact that in most of the exudates the increased response was greater than tenfold. Information as to whether one or both of the phenomena were responsible for the increased activity could be obtained by running a parallel series diluting the original exudate 1 : 10 with sterile exudate.

In general, there was little activity after six hours' exposure in the undiluted exudates. However, in the diluted exudate there were indications of definite activity at six hours, this again being especially true of the acridine.

There were indications of a synergistic or additive effect of acridine in two of the exudates. In general, however, the response obtained when the acridine was used in combination with penicillin, streptomycin or sulfadiazine was no better than when the acridine was used alone.

SUMMARY

The in vitro effectiveness of 5-aminoacridine on five exudates from induced peritonitis in dogs was compared in various ways with that of streptomycin, penicillin, sulfadiazine and various combinations of these drugs.

In the concentrations used, 5-aminoacridine was found to be just as effective or more so than penicillin, streptomycin or sulfadiazine. Furthermore, the acridine effectiveness appeared to be more consistent.

There were only slight indications of a synergistic or additive effect of acridine. In most cases, when the drug was used in combination the effect was no better than when acridine was used alone.

RIGHT THORACOABDOMINAL APPROACH FOR PORTACAVAL ANASTOMOSIS

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WHIPPLE [1] and Blakemore [2] in 1943 began to restudy the problem of the surgical approach to the distressing complications of portal cirrhosis. Eck [3] initiated the study in 1877 when he performed the first recorded successful anastomosis of the portal vein to the inferior vena cava. It remained for Blakemore,[4] Whipple [5] and later Blalock,[6] Linton [7] and others [8] to devise varied shunts between the portal and caval systems and to perfect the technics of the procedures, as well

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2. Blakemore, A. H., and Jere, W. L., Jr.: The Technic of Using Vitallium Tubes in Establishing Portacaval Shunts for Portal Hypertension, Ann. Surg. **122**:476-489, 1945.

3. Eck, N. V.: The Ligature of the Portal Vein, Voyeno Med. J., 1877, cited by Whipple.[1]

4. (*a*) Blakemore, A. H.: Portacaval Anastomosis: A Report of 14 Cases, Bull. New York Acad. Med. **22**:254-263, 1946; (*b*) Operation of Portacaval Anastomosis: Indications, New York State J. Med. **47**:479-485, 1947; (*c*) Indications for Portacaval Anastomosis: Analysis of Cases, Surg., Gynec. & Obst. **84**:645-653, 1947; (*d*) Portacaval Anastomosis: Observations on Technic and Postoperative Care, S. Clin. North America **28**:279-289, 1948; (*e*) Portacaval Anastomosis, Surg., Gynec. & Obst. **87**:277-279, 1948; (*f*) Portacaval Anastomosis, Surgery **24**:480-484, 1948; (*g*) The Portacaval Shunt in the Surgical Treatment of Portal Hypertension, Ann. Surg. **128**:825-842, 1948.

5. Whipple, A. O.: The Rationale of Portacaval Anastomosis, Bull. New York Acad. Med. **22**:251-253, 1946.

6. Blalock, A.: The Use of Shunt or By-Pass Operations in the Treatment of Certain Circulatory Disorders, Including Portal Hypertension and Pulmonary Stenosis, Ann. Surg. **125**:129-141, 1947.

7. Linton, R. R.; Chester, M. J., and Volwiler, W.: Portal Hypertension: The Treatment by Splenectomy and Splenorenal Anastomosis with Preservation of the Kidney, S. Clin. North America **27**:1162-1170, 1947. Linton, R. R.: Portacaval Shunts in the Treatment of Portal Hypertension, New England J. Med. **238**:723-727, 1948. Linton, R. R.; Hardy, I. B., and Volwiler, W.: Portacaval Surgery in the Treatment of Portal Hypertension, Surg., Gynec. & Obst. **87**:129-144, 1948.

8. Welch, C. S.: A Technique for Portacaval Anastomosis (Eck Fistula), Surg., Gynec. & Obst. **85**:492-494, 1947. Heaney, J. P., and Humphreys, G. H., II: The Right Thoraco-Abdominal Approach, Ann. Surg. **128**:948-955, 1948. Pattison, A. C.: Use of Portacaval Anastomosis in Portal Cirrhosis, Arch. Surg. **58**:590-602 (May) 1949.

as the indications for their use. The technical feasibility of such anastomoses, as well as the rationale for their choice, has been established. Because of the large stoma and the lessened chance for thrombus formation most authors favor the end to side portacaval shunt. The following communication describes the use in two cases of such an anastomosis, as well as the advantages of the right thoracoabdominal approach to the portacaval area.

Blakemore [4g] and Satinsky,[9] writing independently, suggested the use of the right thoracoabdominal incision (fig. 1 *a*) to supplant the customary anterior abdominal approach to the portal vein area. The portal vein and inferior vena cava are located deep in the upper area of the abdomen, and the site for the anastomosis of these two vessels is recessed under the caudate lobe of the liver and the costal arch. Exposure of the vessels may be so difficult by the anterior approach that anastomosis must occasionally be haphazardly performed or else abandoned entirely. Through

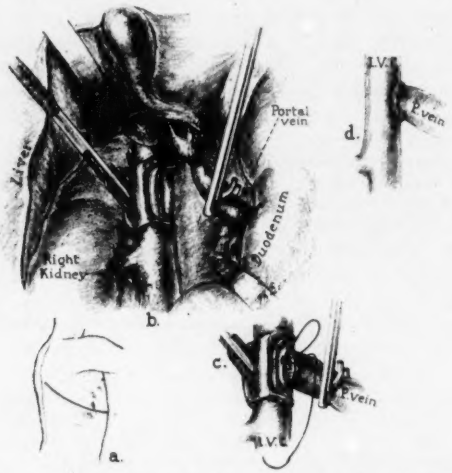

Fig. 1.—Drawings of portacaval shunt performed through a right thoracoabdominal incision. Insert *a* shows the position of the patient on the operating table and the site for the incision. Insert *b* shows the exposure of the retroduodenal fossa and the application of the Potts-Smith and Blalock clamps. A ligature has been placed at the bifurcation of the portal vein preparatory to transection of the vessel. The common bile duct and the hepatic artery are retracted in the hepatoduodenal ligament. Insert *c* shows the end to side anastomosis between the stump of the portal vein and the incised vena cava. An everting continuous 30 inch (76 cm.) suture of 00000 silk is used for the anastomosis. Insert *d* shows the completed anastomosis.

the right thoracoabdominal approach (fig. 1 *b*) one directly views the portal vein and inferior vena cava without the necessity of retracting any structure other than the caudate lobe of the liver, if that organ is greatly enlarged. The diaphragmatic extension of the incision allows for displacement of the liver out of the field and into the thorax. With the patient in the lateral position, the portal vein is the most accessible vessel in the hepatoduodenal ligament; thus, the common duct need not be dissected free or the hepatic artery even visualized. In addition, the thoraco-

9. Satinsky, V. P.: Thoraco-Abdominal Approach for Portacaval Anastomosis, Ann. Surg. **128**:938-947, 1948.

abdominal incision lays open a much larger field so that the portal vein may be mobilized over a greater length and in suitable cases a side to side anastomosis performed.

In the two cases herein reported the right thoracoabdominal incision was started at the lateral border of the right erector spinae muscle and carried through the bed of the ninth rib to the lateral edge of the right rectus abdominis muscle. With the use of endotracheal anesthesia, the thorax and lateral portion of the abdominal wall were opened, and the diaphragm was incised in the line of its fibers as far as the hepatic vein. After dislocation of the liver into the lower region of the thorax, the vascular shunts from the bed of the liver to the omentum were severed; the control of hemorrhage from these vessels was tedious and effected by sutures and oxycel* gauze. The inferior vena cava was mobilized from the right renal vein almost to the diaphragm. The hepatoduodenal ligament was then incised along its lateral edge and the portal vein mobilized from its origin cephalad to the place of entrance of its right and left branches into the substance of the liver. Because of the extreme induration in the hilus of the liver, the portal vein in each case was severed at its division into right and left branches; Satinsky [9] suggests that the branches be separately ligated as high as possible in the liver so as to diminish the chance of extensive thrombus developing in the stumps. It would appear that thrombosis occurs regardless of the level of transection of the vein. Certainly, in indurated liver tissue such as that encountered in these two cases there would be the added hazard of injuring not only the vein but the liver as well if the right and left branches of the portal vein were separately ligated. Hence, the portal vein was transected at its division in the hilus of the liver (fig. 1 *b*): the upper end was ligated and a Blalock clamp [10] was applied to the lower end. The portal vein was mobilized, and in each case one small branch arose from the anterior inferior surface of the pancreas to enter the vein. A modified Potts-Smith clamp [11] was then placed on the inferior vena cava. This clamp was preferred to those demonstrated by Blakemore [4g] and by Bing [12]; the Potts-Smith clamp, besides effecting hemostasis in the edge to be anastomosed, allows an uninterrupted flow of blood through the vena cava. In addition, the clamp does not slip and is not awkward to handle in the wound. An end to side anastomosis was then performed by means of a continuous everting suture of 00000 braided silk on an atraumatic curved needle (fig. 1 *c* and *d*). Cotton suture technic was used throughout and the wounds were closed without drainage. Three thousand five hundred to 4,000 cc. of blood was used in each procedure, and the patients tolerated the operation without difficulty.

REPORT OF CASES

CASE 1.—On Jan. 16, 1949, a 53 year old white man complaining of severe, progressive ascites was admitted to Akron City Hospital and the service of Dr. M. R. Schwartz. The patient gave a history from 1930 to 1947 of a daily consumption of at least 1 pint (500 cc.) of whisky but claimed abstinence from alcohol from 1947 to 1949. In June 1947 and December 1948 he was

10. Blalock, A., and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in Which There Is Pulmonary Stenosis or Atresia, J. A. M. A. **128**:189-202 (May) 1945.

11. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of the Aorta to a Pulmonary Artery in Certain Types of Congenital Heart Disease, J. A. M. A. **132**:627-631 (Nov. 16) 1946.

12. Bing, R. J.; Handelsman, J. C.; Campbell, J. A.; Griswold, H. E., and Blalock, A.: The Surgical Treatment and the Physiopathology of Coarctation of the Aorta, Ann. Surg. **128**:803-824, 1948.

hospitalized because of acute exsanguinating gastrointestinal hemorrhages: on these occasions he regurgitated bright blood and passed copious tarry stools. In the interval between these admissions he had often passed tarry stools. Ascites, first noted in December 1948, became progressively severer and was temporarily relieved by abdominal paracentesis. There was no history of jaundice. Since June 1947 the patient had been maintained on a vigorous modern medical regimen for the treatment of cirrhosis.

Physical examination on Jan. 16, 1949, revealed a pendulous abdomen (fig. 2) and a rather severe degree of pitting edema of the feet in a patient suffering wasting of the upper half of his body. The abdominal veins were dilated, and numerous spider angiomas were present. After removal of 9,400 cc. of ascitic fluid the liver edge was palpable as a grossly nodular, hard, rounded ridge three fingerbreadths below the costal margin. The spleen was not palpable. Significant laboratory findings included 5.5 Gm. of serum protein per 100 cc.; an albumin-globulin ratio of 2.4:1; sulfobromophthalein retention, 30 minutes, 10 per cent; prothrombin

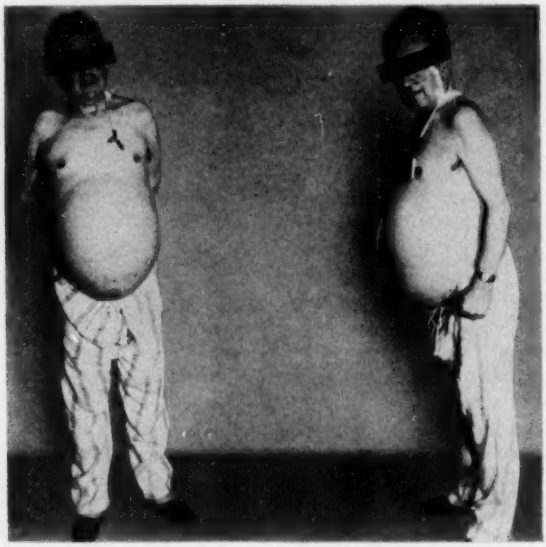

Fig. 2.—Photographs of patient R. T. (case 1). Note the severe abdominal distention and the wasting of the upper extremities. The nasogastric tube is of soft rubber and is left in situ for the administration of a constant drip of a high protein, high calory solution.

time 47 per cent of normal; cephalin flocculation negative, and blood and spinal fluid reactions negative. The presence of esophageal varices was demonstrated by esophagram (fig. 3).

The patient was maintained for three weeks on a vigorous medical regimen including amino acids, vitamins, blood transfusions and intravenous injections of intraheptol® (Lederle). He received a daily nasogastric tube feeding mixture containing from 4,000 to 6,000 calories; in each 1,000 cc. of this mixture there were 1,426 calories derived from the contained 102 Gm. of carbohydrate, 61 Gm. of protein and 86 Gm. of fat. During the last two weeks of this three week period ascitic fluid reformed rapidly; 10,000 cc. was aspirated at each of three paracenteses. At the end of this rehabilitation period significant laboratory findings included 6.3 Gm. of serum protein per 100 cc., with one value at 6.9 Gm.; albumin-globulin ratio 2.3:1; prothrombin time 68 per cent of normal; blood cholesterol 182 mg. per 100 cc., and cholesterol esters 66 mg. per 100 cc. It was apparent that liver function was adequate for the maintenance of a satisfactory protein and prothrombin level. However, the protein exsanguination from rapidly recurring ascites and the dangerous repeated episodes of esophageal hemorrhage indi-

cated an increase in the severity of the degree of portal hypertension. This increase together with a rapid deterioration in the general physical condition of the patient occurred in spite of a long trial on a modern medical regimen for cirrhosis. If the patient was to be saved, it appeared necessary to by-pass the portal circulation around the liver.

On Feb. 10, 1949, with the patient under endotracheal anesthesia, a right thoracoabdominal incision was made after resection of the ninth rib and an end to side portacaval shunt (fig. 1) performed. The liver was hard, nodular and of normal size; the spleen was tense and approximately 50 per cent larger than normal; the portal pressure was approximately 400 mm. of water. After an uneventful operation and postoperative course, the patient was discharged from the hospital on his fourteenth postoperative day. At that time the cephalin flocculation had increased to 3 plus, and the serum protein dropped to 4.9 Gm. per 100 cc., with an albumin to globulin ratio of 1:1. However, the prothrombin time was 51 per cent of normal, and the red and white blood cell counts were maintained at normal ranges. In addition, the ascites and edema disappeared, and there was no recurrence of the melena.

CASE 2.—On March 19, 1949, after a hematemesis of almost 1 quart (1,000 cc.) of bright red blood a 37 year old white man was admitted to Akron City Hospital on the service of

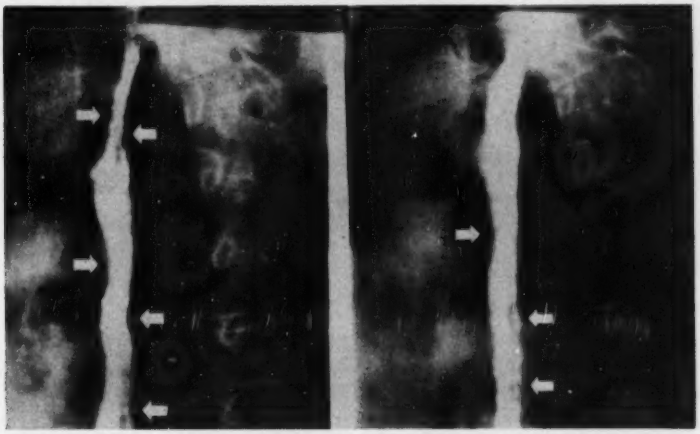

Fig. 3 (case 1).—Esophagrams of patient R. T. illustrating esophageal varices.

Dr. R. T. Yoshikawa. The patient gave a 15 year history of the daily consumption of one or two cases of beer and the sporadic drinking of large volumes of whisky. In 1946 ascites first appeared; it periodically recurred in spite of the fact that the patient almost stopped drinking alcoholic beverages and was maintained on active medical therapy for his cirrhosis. In February 1948 peritoneoscopy revealed the presence of typical atrophic cirrhosis, and since that time the patient had received modern cirrhosis medical therapy including amino acids, intravenous injections of intraheptol,* vitamins and a high protein diet. There was no history of jaundice, and this was the initial episode of melena.

Physical examination on March 19 revealed a pale, emaciated, chronically ill white man (fig. 4) appearing much older than his stated age of 37. The abdomen was distended by ascites, and there was distention of the veins of the abdominal wall. A severe degree of pitting edema of the feet was present. After the removal of 4,500 cc. of ascitic fluid the hard liver edge was palpable three fingerbreadths below the ziphoid process. The spleen, palpable two fingerbreadths below the left costal margin, was as firm as the liver. Significant laboratory findings included a red blood cell count of 2,000,000; serum protein 6.3 Gm. per 100 cc.; albumin to globulin ratio 1:1; sulfobromophthalein retention, 30 minutes, 30 per cent; prothrombin time 100 per cent of normal, and cephalin flocculation 2 plus. The presence of esophageal varices was demonstrated by esophagram (fig. 5).

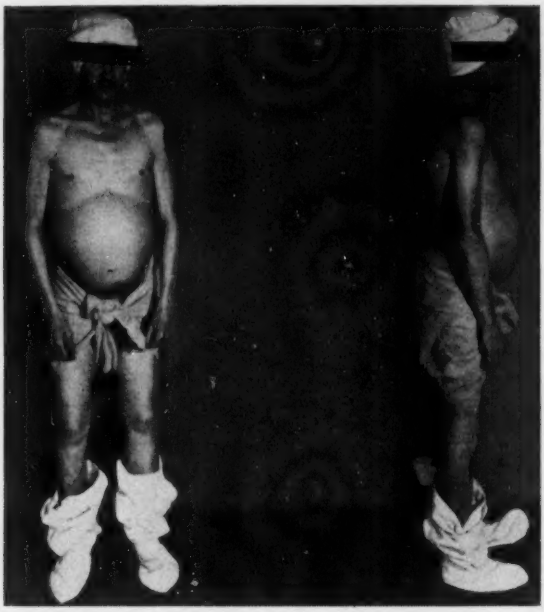

Fig. 4 (case 2).—Photographs of patient R. D. Note the severe abdominal distention and wasting of the upper extremities.

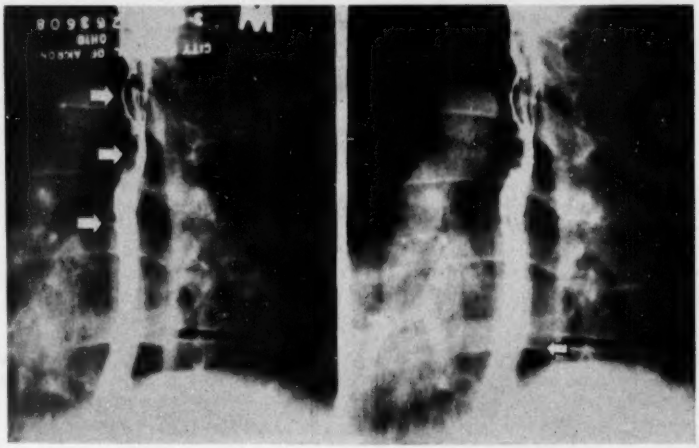

Fig. 5 (case 2).—Esophagrams of patient R. D. illustrating esophageal varices extending high into the thoracic portion of the esophagus.

The patient was maintained for three weeks on the same vigorous rehabilitation regimen described in case 1. The patient's physical condition improved during this period; however, ascites rapidly recurred, and on two occasions 5,000 cc. was withdrawn. At the end of this three weeks significant laboratory findings included a red blood count of 3,600,000; serum protein 6.3 Gm. per 100 cc.; albumin to globulin ratio 1:1; prothrombin time 100 per cent of normal, and sulfobromophthalein retention, 30 minutes, 15 per cent. Liver function thus was demonstrated to be adequate for the maintenance of a normal prothrombin time and serum protein level; however, severe liver damage was indicated by the inability to increase the albumin-globulin ratio above 1:1 and also by the persistence of a cephalin flocculation ranging from 2 to 3 plus. As in case 1, a severe and increasing degree of portal hypertension was indicated by the rapidly recurring ascites and by the hemorrhage (near fatal) from esophageal varices. Clinical observation revealed a rapid deterioration in the patient both physically and emotionally; he had become convinced that he could not long endure such distressing signs of portal hypertension, and he was equally certain that he did not care to live under such conditions.

On April 13, 1949, with the patient under endotracheal anesthesia using a technic identical with that already described (fig. 1), an end to side portacaval shunt was performed. The liver, one and a half times the normal size, was hard, smooth and covered by a dense, tough, glistening, hyalinized capsule, the so-called zuckerguss or sugar-coated liver; the spleen was similarly covered and twice the normal size. The portal pressure was 420 mm. of water; after the opening of the shunt the pressure dropped to 310 mm. of water. The operative procedure was made technically difficult by the extension of the hyalinization of the liver capsule onto the hepatoduodenal ligament; mobilization of the portal vein through such indurated, thickened tissue was an extremely tedious task. In addition, an enlarged caudate lobe prevented ready access to the adrenal portion of the inferior vena cava and thus made difficult the placing of sutures in the anastomosis. The postoperative course was marked by a partial paralytic ileus and by a transitory icterus; the patient was discharged on his sixteenth postoperative day. At that time the cephalin flocculation had increased to 3 plus, and the serum protein dropped to 5.6 Gm. per 100 cc., with an albumin to globulin ratio of 0.9:1. The blood cholesterol was 125 mg. per 100 cc., with 53 per cent cholesterol esters. The red and white blood cell counts were maintained at normal levels. The ascites and edema disappeared, and there has been no recurrence of the melena.

CONCLUSIONS

The advantages and technics of the portacaval shunt operation performed through a right thoracoabdominal incision are described and illustrated with the case histories of two patients on whom this procedure was performed for the relief of portal hypertension.

CARCINOID OF THE RECTUM

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CHARLESTON, S. C.

CARCINOIDS of the gastrointestinal tract are relatively uncommon. These tumors are most frequently found in the appendix, and Foot [1] reports that 0.46 per cent of all appendixes removed for appendicitis were found to contain carcinoid tumors. The next commonest site for carcinoid tumors is the small bowel, and especially the terminal portion of the ileum. Grimes and Bell [2] and Pearson and Fitzgerald [3] have published recent excellent reviews on the subject. Carcinoid tumors have also been reported in the stomach, duodenum, gallbladder, colon and Meckel's diverticula. The rectum is one of the least common locations of this lesion. Horn [4] in 1949 reviewed thoroughly all previously reported cases of carcinoid of the rectum and added six more to the literature. So far as is known to us, there have been 64 cases of carcinoid of the rectum reported or mentioned in the world literature up to the present time. The tumors are no doubt commoner than this figure would indicate, since Ehrlich and Hunter,[5] in a study of 813 gastrointestinal tumors in patients of military age, found 10 carcinoids of the rectum.

The pathologic picture of carcinoids has been thoroughly described by Stout,[6] Horn,[4] Pearson and Fitzgerald [3] and others. They were formerly called argentaffinomas and are believed to be derived from the Kultschitzky cells in the crypts of Lieberkühn. Stout,[6] however, has shown that some carcinoid tumors do not take the silver stain, and he believes that these lesions are derived from the same cells in the "pre-enterochrome" phase. Commonly, carcinoids consist of densely packed masses of rather small cells with clear cytoplasm and small central nuclei and without much pleomorphism. Nevertheless, the histologic picture is rather variable, and many of the reported tumors, especially in the large bowel, show formation of alveoli.

From the Departments of Surgery and Pathology and the Cancer Clinic of the Medical College of the State of South Carolina and the Roper Hospital.

1. Foot, N. C.: Pathology in Surgery, Philadelphia, J. B. Lippincott Company, 1945.

2. Grimes, O. F., and Bell, H. G.: Carcinoid Tumors of the Intestine, Surg., Gynec. & Obst. **88**:317-325, 1950.

3. Pearson, C. M., and Fitzgerald, P. J.: Carcinoid Tumors: A Re-Emphasis of Their Malignant Nature: A Review of 140 Cases, Cancer **2**:1005-1026, 1949.

4. Horn, R. D., Jr.: Carcinoid Tumors of the Colon and Rectum, Cancer **2**:819-837, 1949.

5. Ehrlich, J. C., and Hunter, O. B., Jr.: Tumors of the Gastrointestinal Tract: A Survey of 813 in Persons of Military Age During World War II, Surg., Gynec. & Obst. **85**:98-106, 1947.

6. Stout, A. P.: Carcinoid Tumors of the Rectum Derived from Erspamer's Pre-Enterochrome Cells, Am. J. Path. **18**:993-1009, 1942.

Carcinoid tumors appear to arise from the submucosa and invade the adjacent mucosa and muscularis. The present consensus of writers on the subject is that all carcinoids are probably malignant, although they grow slowly. It is thought that metastases from appendical carcinoids are never seen because the tumor results in obstruction of the lumen of the organ and in symptoms of acute appendicitis, and the appendix is therefore removed before metastases occur. Metastases from bowel carcinoid occur late in the course of the disease, but it has been repeatedly reported [2] that in the presence of distant metastasis removal of the primary focus has resulted in a symptom-free interval of many years. Pearson and Fitzgerald [3] have recently reemphasized the importance of regarding all carcinoids as malignant lesions.

Practically all the articles concerned with carcinoid of the rectum have been written predominantly from the point of view of the pathologist, with histologic characteristics and variants being emphasized much more than therapy and prognosis. A review of the reported cases of carcinoid of the rectum from the clinician's viewpoint seemed to be of some interest. Therefore, the purpose of the present communication is to present a summary of all known cases of carcinoid of the rectum, emphasizing available clinical data, as well as to add two other cases of carcinoid of the rectum to the literature.

The known details concerning the reported lesions are given in the accompanying table. Unfortunately, 16 of the known cases are only mentioned in the literature, no details being given. Among the remaining 50 cases, the lesion was incidentally found at autopsy in 10 and in specimens of bowel removed for carcinoma in 3 others; in none of these 13 cases was metastasis mentioned. There thus remain 37 cases available for more detailed study.

The age of the patients with carcinoid of the rectum varied from 14 to 71 years, and there appeared to be no significant difference in incidence between the sexes. The majority of the patients had no symptoms referable to the local lesion, the lesions being discovered on routine rectal or proctoscopic examination. Symptoms, when recorded, usually included bloody stools and occasionally constipation, tenesmus and lower abdominal pain.

Most of the lesions were small (less than 1 cm. in diameter) and lay in the lower part of the rectum, covered with mucosa. A small number were polypoid and pedunculated, but by far the larger number were sessile. In only three cases (incidental autopsy findings in two) were multiple lesions found. Among all the 66 known cases, metastases have been recognized in only 6 (9.1 per cent). One of these (reported by Siburg [7]) involved a 71 year old man who presented himself with a large abdominal mass and died suddenly and without explanation. At autopsy a carcinoid tumor of the rectum, with metastases to regional lymph nodes, vertebrae and liver, was found. Another patient (reported by Koch [8]) had an extensive infiltrative annular lesion at the 3 cm. level, and because of obstruction a colostomy was done. At autopsy eight months later, metastases to the liver and the lymph nodes were found. Pearson and Fitzgerald [9] reported two cases with metastases. In one

7. Siburg, F.: Über einen Fall von sogenanntem Karzinoid des Rektums mit ausgedehnter Metastasenbildung, Frankfurt. Ztschr. f. Path. **37**:254-269, 1929.

8. Koch, F.: Maligne Carcinoide, Chirurg **12**:270-275, 1940.

9. Pearson, C. M., and Fitzgerald, P. J.: Carcinoid Tumors of the Rectum: Report of 3 Cases, 2 with Metastases, Ann. Surg. **128**:128-143, 1948.

Summary of Reported Cases of Rectal Carcinoid

No.	Author and Date	Age, Sex	Symptoms	Metastases	Treatment	Follow-Up	Comment
1	Saltykow, S.: Beitr. z. path. Anat. u. z. allg. Path. **54**:559, 1912	28, F	.....	None	.....	.....	5 mm.; 5 cm. level; incidental autopsy finding
2	Reichel, P., and Staemmler, M.: Neue deutsche chir. **33a**:230, 1924	35, F	.....	.....	.....	.....	Nodule (pea sized) 10 cm. level; no other details given
3	Martin, J. F., and Dechaume, J.: Lyon méd. **133**:686, 1924	50, M	None	None known	Local excision	.....	Incidental finding; patient had anal fissure; pedunculated lesion 3 cm. level on anterior wall and sessile lesion adjacent
4	Siburg,[7] 1929	71, M	.....	Lymph nodes vertebrae liver (autopsy)	.....	.....	Had large palpable abdominal mass
5	Brunschwig, A.: J. A. M. A. **100**: 1171 (April 15) 1933	63, M	None	None known	Local excision	None	Incidental finding in routine examination; submucosal nodule 0.5 cm. in diameter, 8 cm. level anterior
6 to 10	Feyrter, F.: Ergebn. d. allg. Path. u. path. Anat. **29**:305, 1934	14, M 54, F 56, F 59, F 67, F	.....	None	.....	.....	Incidental autopsy findings
11	Humphreys, E. M.: Am. J. Cancer **22**:765, 1934	28, M	.....	.....	.....	.....	No details given
12	Koch,[8] 1940	64, M	Diarrhea, constipation and tenesmus	Lymph nodes, liver (autopsy)	Colostomy for obstruction	Died 8 mo. later	Infiltrative, annular extensive tumor, 3 cm. level
13	Mallory, T. B.: New England J. Med. **222**:806, 1940	....	.....	.....	.....	.....	No details given
14	Ashworth and Wallace,[11] 1941	31, F	Bleeding and constipation	None known	Abdominoperineal resection	None	Polypoid mass 0.7 cm. in diameter, 10 cm. level
15	Stout,[6] 1942 1	19, F	Bleeding and constipation	None known	Local excision	No recurrence 9 yr. later	Polypoid mass 2 cm. diameter, 5 cm. level anterior wall
16	Stout,[6] 1942 2	41, F	Diarrhea and LLQ pain	None known	Local excision	No recurrence 2 yr. later	Patient had regional enteritis; sessile mass 5 mm. diameter, 5 cm. level anterior wall
17	Stout,[6] 1942 3	34, F	Bleeding and painful defecation	None known	Local excision	No recurrence 2 mo. later	Patient had hemorrhoids; sessile mass 1 cm. diameter, 5 cm. level anterior wall
18	Stout,[6] 1942 4	38, F	Bleeding	None known	Local excision	No recurrence 3 yr. later	Sessile mass 5 mm. diameter, anterior wall
19 and 20	Stout,[6] 1942 5 and 6	42, F 43, M	.....	.....	.....	.....	Sessile masses; incidental autopsy findings
21	Helwig, E. B.: Surg., Gynec & Obst. **76**:419, 1943	56, M	.....	None	.....	.....	Submucosal nodule 15 mm. in diameter; incidental autopsy findings
22	Yaker, D. N.: Clinics **3**:1055, 1944	29, M	Obstructive sensation on defecation	None known	Local excision	No recurrence 3 mo. later	Sessile nodule 4 in. level anterior wall
23	Rigdon, R. H., and Fletcher, D. E.: Am. J. Surg. **71**:822, 1946	60, M	None	None	.....	.....	Multiple submucosal nodules; incidental autopsy findings
24	Severance, A. D.: Texas State J. Med. **41**:564, 1946	33, F	None	None known	Local excision	None	Routine examination for vaginal bleeding; submucosal tumor 1 cm. in diameter
25, 26 and 27	Dukes, C. E.: Proc. Roy. Soc. Med. **39**:763, 1946 1, 2, 3	....	.....	None known	.....	.....	All incidental findings in specimens removed for carcinoma

28	Dukes, C. E., 1946 4	40, F	.....	.....	Local excision	None	Nodule just above dentate line
29	Dukes, C. E., 1946 5	37, F	.....	.....	Local excision	No recurrence in 9 yr.	Nodule in lower third of rectum
30	Dukes, C. E., 1946 6	40, M	.....	.....	Local excision	Died 1 yr. later of other causes	.....
31	Dukes, C. E., 1946 7	36, F	.....	.....	Local excision	None	.....
32 and 33	Dukes, C. E., 1946 8 and 9	....	.....	.....	.....	.....	No details given
34 to 43	Ehrlich and Hunter,[5] 1947 10 cases	18- .. 38	.....	None known	Local excision	Indefinite time but no recurrence	.....
44 to 47	Jackman, R. J.: Proc. Staff Meet., Mayo Clin. 22:502, 1947	....	.....	.....	.....	.....	No details given
48	Pearson and Fitzgerald,[3] 1948	51, M	Bloody stools and obstructive symptoms	Lymph nodes, liver, pancreas and perirenal area	Abdominal exploration only	Died 2 yr. after onset of symptoms	3 polypoid nodules in rectum
49	Pearson and Fitzgerald,[3] 1948	45, F	Bloody stools and obstructive symptoms	Liver and para-aortic nodes	Exploration and colostomy only	None	Annular constricting mass at 14 cm. level (rectum fixed at operation)
50	Pearson and Fitzgerald,[3] 1948	69, M	Bloody stools	None known	Local excision	No recurrence 10 mo.	Polyp with pedicle
51	Horn,[4] 1949 8	29, F	None	Liver, lungs, spleen, adrenal and pancreas (autopsy)	None	Died as result of generalized metastases	Symptoms of hepatic insufficiency; small rectal mass 3 x 2 cm. on right lateral wall 1 cm. level
52	Horn,[4] 1949 9	42, F	None	None known	Local excision (implied)	"Short time"	Anal fissure; tumor found on routine proctoscopy
53	Horn,[4] 1949 10	56, F	None	None known	Local excision (implied)	"Short time"	Cystocele and rectocele; tumor found on routine proctoscopy
54	Horn,[4] 1949 11	25, F	None	None known	Local excision (implied)	"Short time"	Fistula in ano; tumor found on routine proctoscopy
55	Horn,[4] 1949 12	.. M	None	None known	Local excision (implied)	"Short time"	Admitted for study of weight loss; tumor found on routine proctoscopy
56	Horn,[4] 1949 13	62, M	None	None known	Local excision (implied)	None	Prolapsed hemorrhoids; tumor found on routine proctoscopy
57	Wilson,[10] 1949	57, M	Rectal bleeding	Single lymph node	Abdominoperineal resection	Died on 22d postoperative day of pulmonary emboli	5 cm. level on left lateral wall 3 cm. in diameter; invasion of muscularis
58 to 64	Pearson and Fitzgerald,[9] 1949	....	.....	.....	.....	.....	No details given
65	Mayo and McKee, 1950	24, F	LLQ pain and rectal bleeding	None known	Local excision	No recurrence 3 mo.	Polyp 1 cm. in diameter 6 cm. level; right lateral wall; stalk 1 cm. in length
66	Mayo and McKee, 1950	29, M	None	None known	Local excision	No recurrence 19 mo.	Tumor found on routine examination; polyp 1 cm. in diameter, 5 cm. level; right posterior lateral wall

there were three polypoid lesions in the rectum, and at abdominal exploration metastases were found in the regional lymph nodes, liver, pancreas and perirenal tissues; the patient died two years after the onset of symptoms. In the other there was an annular constricting mass at the 14 cm. level, and at exploration the rectum was fixed and metastases were found in the liver and the periaortic nodes. A colostomy was done, and the patient was subsequently lost to follow-up. Horn [4] reported on a patient with a rectal mass 3 by 2 cm. who died at the age of 29 as a result of generalized metastases to the liver, lungs, spleen, adrenal and pancreas. An abdominoperineal resection was performed by Wilson [10] on a 57 year old white man, and the lesion was found to invade the muscularis extensively, with a single lymph node metastasis.

Abdominoperineal resection for carcinoid of the rectum has been reported twice. Wilson's patient, mentioned previously, died on his twenty-second postoperative day of pulmonary emboli. The other radical procedure was reported by Ashworth and Wallace.[11] No metastases were found in this case, but no follow-up data are available. Local excision of the lesion has been performed in 30 cases of carcinoid of the rectum. No follow-up data are available for six of these cases. The follow-up intervals in the remaining 24 cases vary between two months and nine years, but to date no recurrence or metastasis has been recognized in any of them.

REPORTS OF CASES

CASE 1.—W. S., a 24 year old Negro woman, was admitted to the hospital on June 21, 1950, because of bloody stools and intermittent pain in the left lower abdominal quadrant of three months' duration. Her past history and a review of the symptoms revealed nothing remarkable. Physical examination was noncontributory except for palpation of a firm nodule in the rectum about 6 cm. above the anal margin. Routine laboratory data were within the limits of normal, and a barium enema with air insufflation failed to demonstrate any other lesion of the large bowel. Proctoscopic examination showed a polyp approximately 1 cm. in diameter attached to a valve on the right lateral wall of the rectum by a stalk 1 cm. in length. With the patient under spinal anesthesia, the stalk was ligated and the polyp removed.

Pathologic Examination.—The gross specimen consisted of two portions of gray tissue, one of polypoid configuration measuring 1.5 cm. in diameter (fig. 1). Histological section (fig. 2) showed polypoid elevation of the rectal mucosa by a submucosal nodular mass of cells which were uniform in character, small and cuboidal, with clear cytoplasm and centrally placed nuclei. The absence of pleomorphism and mitosis was noteworthy. The architectural pattern was one of gradually coiling double columns of cells intermingled with fairly large solid cell masses of similar type. Although there was no demonstrable capsule, the tumor was discrete and restricted in its extent.

The patient was followed for three and a half months, during which time her stools were normal and she was asymptomatic. Proctoscopic examination showed no evidence of recurrence, and the site of the previously excised lesion could not be identified. Abdominal examination showed no abnormalities.

CASE 2.—B. D., a 29 year old Negro, was admitted to the hospital on March 4, 1949, for treatment of an active duodenal ulcer. He had had no symptoms other than those referable to the ulcer. On routine examination, a flat polyp 1 cm. in diameter was noted on the posterior lateral wall of the rectum 5 cm. above the anus. Material from this was removed through the proctoscope for biopsy on March 8, 1949, and the growth reported as probable carcinoid of the

10. Wilson, H.: Carcinoid of the Rectum, Arch. Path. **48**:187-189 (Aug.) 1949.

11. Ashworth, C. T., and Wallace, S. A.: Unusual Locations of Carcinoid Tumors, Arch. Path. **32**:272-276 (Aug.) 1941.

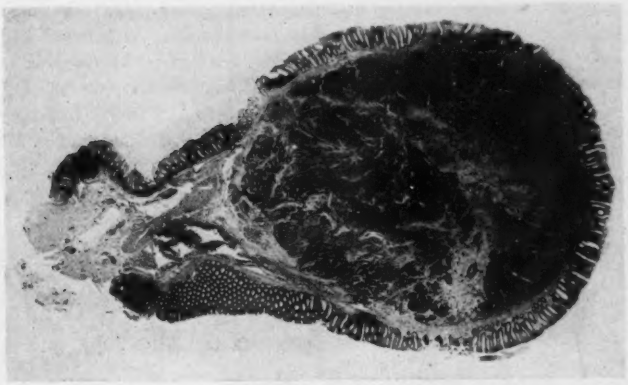

Fig. 1 (case 1).—Photomicrograph of histological section; × 7.

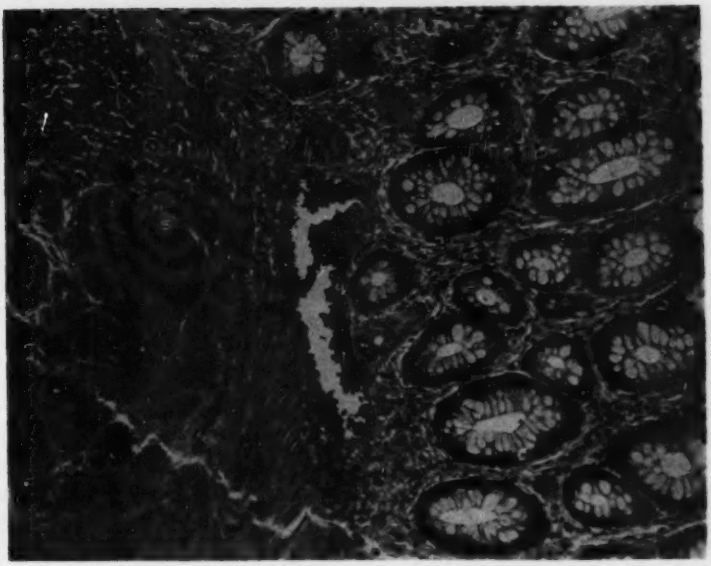

Fig. 2 (case 1).—Photomicrograph of histological section; × 150.

rectum. A barium enema failed to demonstrate any other lesion in the colon. On March 14, 1949, the polyp was excised through the proctoscope, with the patient under spinal anesthesia.

Pathologic Examination.—The gross specimen consisted of a polypoid structure 1 cm. in diameter and showed an area of surface ulceration. Histological sections (fig. 3) showed a picture similar to that noted in case 1. There was an area of surface ulceration, considered to be the site of previous biopsy, and apparent early infiltration by small clusters and cords of these cuboidal cells toward the base of the stalk.

Nineteen months later the patient was asymptomatic and proctoscopic examination showed no evidence of recurrence. The site of the previously excised lesion was identified as a tiny puckered scar.

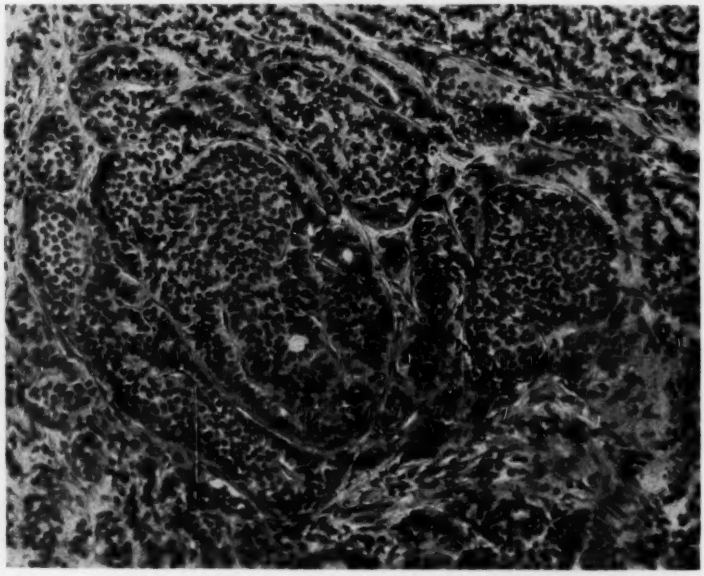

Fig. 3 (case 2).—Photomicrograph of histological section; × 150.

COMMENT

From the summary of clinical data on known carcinoid tumors of the rectum presented above, it would seem that the lesion is one which, while recognizably malignant, ordinarily has a fairly benign course and grows rather slowly. In only 9.1 per cent of the reported cases have metastases been noted. In these the metastasis apparently took place through both lymphatic vessels and blood stream. It is obvious that the follow-up data on the known cases are inadequate, and the importance of recording further follow-up data might be mentioned here. The apparent success of local excision in single lesions would seem to indicate it as the treatment of choice, especially for pedunculated lesions such as the one reported in this communication. However, if there is obvious invasion of the muscularis and the tumor cannot be removed easily *in toto* by local excision or if recurrence develops after

local excision, it is suggested that abdominoperineal resection might be the treatment of choice. For the larger lesions, and especially the occasional annular constricting lesion, such a resection would seem to be definitely indicated.

SUMMARY

A review of reported clinical data on all known cases of carcinoid of the rectum is given and two additional cases added, bringing the total number of known cases to 66. The surgical therapy of carcinoid tumors of the rectum is discussed briefly.

NOTE.—Since this article was submitted for publication, the patients reported here have been followed seven and 22 months, respectively, and no evidence of recurrence has been noted.

Shepard, Strug and DiLeo [12] have recently reported two additional cases of carcinoid of the rectum. The treatment in both cases was abdominoperineal resection, and in neither case were metastases noted.

12. Shepard, R. M., Jr.; Strug, L. H., and DiLeo, J. H.: Carcinoid Tumors of the Rectum, Surgery **29**:205-209, 1951.

DIVERTICULOSIS AND DIVERTICULITIS OF THE VERMIFORM APPENDIX

A Brief Review and Report of Sixteen Cases

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NEW YORK

IN SPITE of the large number of papers written on the subject, diverticulosis and diverticulitis of the appendix are still believed to be rare. While the conditions are not common, one cannot judge their incidence from published reports. The frequency with which they are found will be in direct proportion to the effort expended in searching for them. This was pointed out by Stout,[1] who found five cases in one year with special study, whereas only one case had been reported from the same institution in the previous 10 years. The reported incidence is variable, but the lowest was found by the Army Institute of Pathology, 42 cases among 51,525 appendixes studied, or 0.08 per cent.[2] The highest was reported by Mertens,[3] 2.8 per cent. This paper is being presented in order to draw attention to this condition and to report 16 cases.

ETIOLOGY AND PATHOLOGICAL PHYSIOLOGY

Diverticula are outpocketings of the wall of the appendix and are divided into true and false. The true ones have all the layers of the normal appendix, while the false lack the muscularis. The majority of these diverticula occur at the mesenteric border, and they are commonest at the distal third of the appendix.

A great deal has been written and strong views expressed about the various theories as to the causation of diverticula of the appendix. It is likely that more than one factor exists in each case and that these various ideas are complementary rather than at odds. All writers agree that weakening of the wall of the appendix is essential to the condition. This weakening is produced by destruction of the muscularis, which is subsequently replaced by scar tissue. It may be due to focal infection, to injury with superimposed infection (foreign bodies, fecaliths, twisting) in which the mucosa may regenerate but the muscularis is replaced by fibrous tissue [4] or to a defect in the wall at the site where the blood vessels penetrate the

From the Department of Laboratories, Lebanon Hospital.

1. Stout, A. P.: A Study of Diverticulum Formation in the Appendix, Arch. Surg. **6**:793-829 (May) 1923.

2. Army Institute of Pathology: Personal communication to the authors, 1949.

3. Mertens, V. E.: Falsche Divertikel der Flexura sigmoidea und des Processus vermiformis, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **9**:743-761, 1902.

4. Collins, D. C.: Diverticula of the Vermiform Appendix: A Study Based on 30 Cases, Ann. Surg. **104**:1001-1012, 1936. Kline, B. S.; Young, A. M., and Straus, R.: False diverticulum Formation Following Acute Perforative Appendicitis, Arch. Path. **31**:25-36 (Jan.) 1941. Sauer, P. K.: Diverticula of the Appendix, Am. J. Surg. **10**:564-570, 1930. Stout.[1]

bowel wall.[5] The next factor is obstruction of the lumen, which may be either partial or complete.[6] It may be caused by swelling of the mucosa, inflammation, fecaliths, fibrous strictures, torsion and the like. It will be noted that many of the factors are common both in causing weakness of the wall and in producing obstruc-

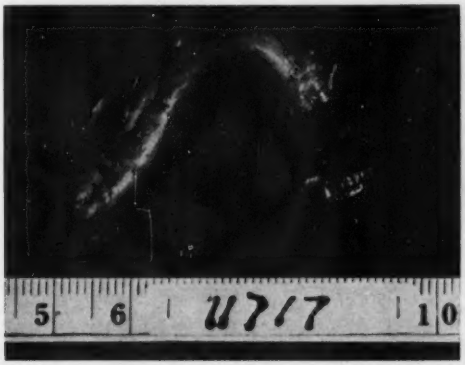

Fig. 1.—A large solitary diverticulum near the base of the appendix near the mesentery side.

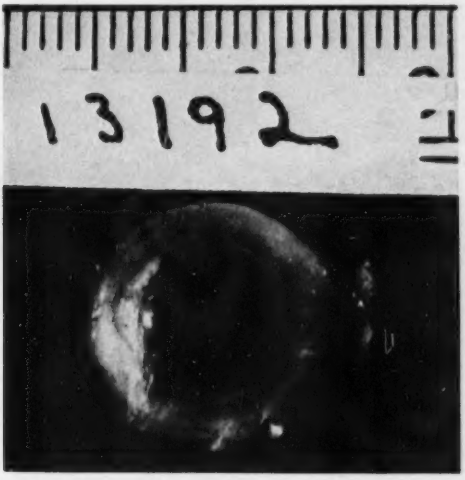

Fig. 2.—Cross section of a diverticulum. Notice the defect in the wall which leads to the diverticulum.

5. Klebs, E.: Handbuch der pathologischen Anatomie, Berlin, A. Hirschwald, 1869, vol. 1, p. 271. Mertens.[3]

6. Stewart, J. D.: Diverticulosis of the Appendix, New England J. Med. **203**:1288-1290, 1930. Stout.[1]

tion. Buirge and his co-workers [7] have demonstrated that the appendix in the human being secretes from 1 to 2 cc. daily. This continuing secretion in the face of obstruction leads to increasing pressure within the lumen of the appendix, which is augmented by the contractions of the appendix in its efforts to empty itself.[1]

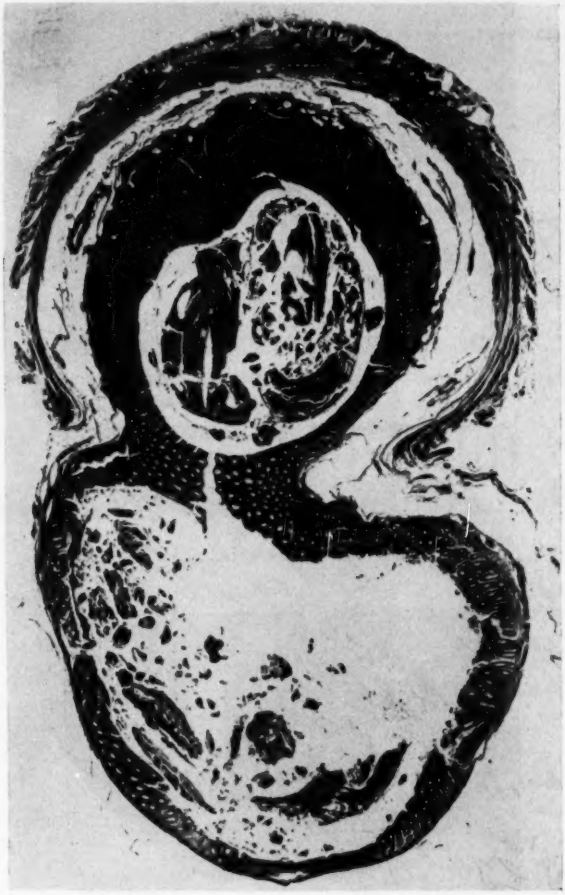

Fig. 3.—Low power photomicrograph of a diverticulum of the appendix without evidence of inflammation. The absence of muscularis is clearly demonstrated.

The diminished secretion associated with advancing age is probably a factor in the diminished incidence of appendicitis in old age. The appendical wall gives way

7. Buirge, R. E.; Dennis, C.; Varco, R. L., and Wangensteen, O. H.: Histology of Experimental Appendical Obstruction (Rabbit, Ape and Man), Arch Path. **30**:481-503 (Aug.) 1940.

at its weakened point because of these forces, thus producing a diverticulum (false). Continued activity of these factors leads to ulceration and/or infection and may culminate in perforation of the diverticulum. Stout [1] produced diverticula of the appendix experimentally in dogs by increasing the intraluminal pressure after weakening the wall. Since perforation of the appendix is certain to result in a defect, Gramse and others [8] studied appendixes removed after known episodes of perforation. They found an incidence of 74.4 per cent of diverticula. This is further support for the above concepts of the cause. In view of the known tendency for diverticulitis to progress rapidly and since previous infections are such an impor-

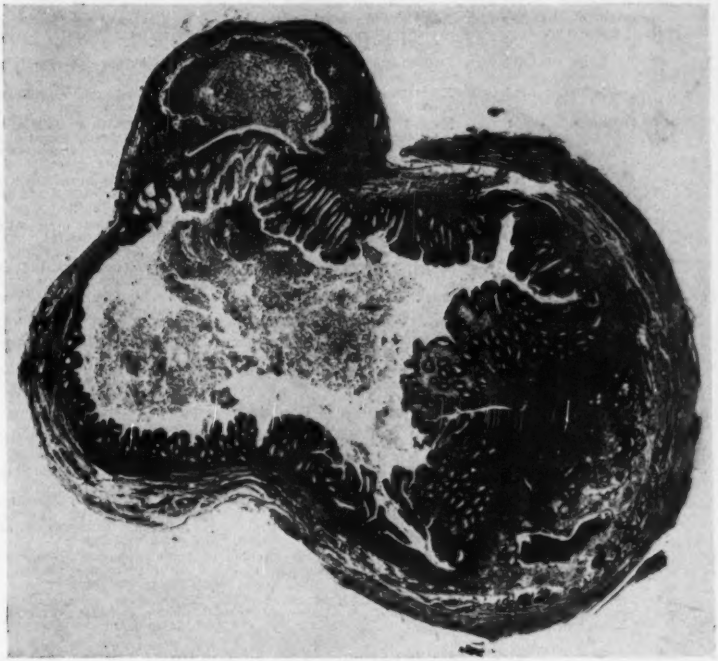

Fig. 4.—Low power photomicrograph of a severely inflamed diverticulitis of the appendix. The absence of muscularis in the diverticulum is obvious.

tant factor in their causation, it is well to emphasize again the importance of removing appendixes after repeated attacks and especially after known perforations.

COMMENT ON CASES REPORTED

Sixteen cases were found in our records at Lebanon Hospital (table). Analysis of these cases revealed the following facts: The ages varied from 3 to 70 years,

8. Gramse, A. E.; Dockerty, M. B., and Waugh, J. M.: False Diverticula of the Appendix: A Sequel of Previous Inflammation and Rupture of the Appendix; Clinical and Pathological Study, S. Clin. North America **29**:1189-1207, 1949.

with a mean of 34 years. This is in accord with other reports, which place the largest number of patients between 20 and 40 years of age. The patient who was 3 years old appears to be the youngest reported to date. There were 10 males (62.5 per cent) and 6 females (37.5 per cent). All but two of the diverticula occurred on the mesenteric border of the appendix. It is noteworthy that in only four of these cases was a diverticulum noted by the surgeon (cases 1, 7, 8, 9), and in

Summary of Pertinent Findings in the Reported Cases

Case	Age and Sex	Previous Attacks	Duration of Symptoms	Operative Description of the Appendix	Pathological Report
1	54 M	Abdominal pains 10 yr.	10 yr.	Adhesions around the appendix; obliteration of tip and a pouch seen	Typical small appendical diverticulum
2	23 M	None	24 hr.	Swollen and twisted on itself with a bulbous tip	Acute diffuse appendicitis with diverticulum
3	13 F	6 in 3 yr.	24 hr.	Edematous with localized abscess surrounding it	Acute phlegmonous appendicitis with diverticulum
4	32 F	None	?	Marked thickening of the appendix with a fecalith	Thickened with lumen filled with fibrofatty replacement of mucosa and partial obliteration; diverticulum present
5	34 M	Many	24 hr.	Gangrenous appendix with appendical abscess	Acute diffuse appendicitis with acute diverticulitis and obliteration of lumen
6	7 M	Many	48 hr.	Gangrenous tip with perforation	Acute gangrenous appendicitis with diverticulum; fecalith with pinpoint lumen
7	32 M	Many	?	Acutely inflamed with diverticulum	Acute inflammation and acute diverticulitis
8	37 M	None	7 hr.	Small thin-walled diverticulum at base with inspissated feces; wall appears hemorrhagic	Diverticulum of appendix with bluish color
9	34 M	?	24 hr.	Acute diverticulitis with multiple diverticula	Acute diverticulitis of appendix with diverticulosis
10	70 M	?	48 hr.	Gangrenous appendix, many adhesions, local abscess	Acute suppurative appendicitis with periappendicitis and acute diverticulitis
11	3 F	2 wk.	24 hr.	Acute inflammation with distal end clubbed, thickened and adherent to terminal ileum	Acute diverticulitis of the appendix
12	40 F	?	72 hr.	Gangrenous with perforation at midportion	Acute suppurative appendicitis, diverticulum of appendix with fecalith
13	18 F	?	72 hr.	Retrocecal with abscess around the tip	Acute suppurative appendicitis; diverticulitis of appendix; periappendicitis; partial obliteration of lumen
14	62 M	?	96 hr.	Acutely inflamed with tip in mass of omentum and perforated	Acute suppurative appendicitis with acute diverticulitis and periappendicitis
15	40 M	Appendicular abscess 7 mo. previously	48 hr.	Acutely inflamed, retrocecal and adherent	Suppurative appendicitis with periappendicitis; diverticulum of appendix
16	47 F	None	24 hr.	Acutely inflamed	Acute gangrenous diverticulitis with periappendicitis, narrowing at middle and dilatation of tip

two of these there was no acute inflammation. The severity of the disease affecting these appendixes is noted as being far beyond the usual degree found in a series of cases of acute appendicitis, and this probably explains part of the difficulty in noticing this condition at operation. The extension of these diverticula into the mesoappendix also makes them more difficult to recognize at the operating table and when they are being sectioned in the pathological laboratory. Multiple and closely spaced serial sections would help find these, but this is not practical as a routine measure in most laboratories. If I exclude cases 1 and 4, in which the appendix was removed incidentally during other procedures, it will be seen that

in 11 of the remaining 12 cases there were severe pathological processes. Two of the patients had symptoms less than 24 hours, but perforation with abscess formation was already found. These findings are in accord with the known tendency for rapid progression of the disease in diverticulitis. In case 15 there was recurrent appendicitis following a known perforation of the appendix 7 months before, and the finding of a diverticulum was to be expected.[8] In almost every case there was evidence of previous disease or some form of obstruction either at operation or on pathological examination. There were no deaths in this series.

SUMMARY AND CONCLUSIONS

1. The incidence of diverticulitis and diverticulosis of the appendix will vary directly with the care exercised in searching for these conditions.

2. Weakening of the wall by infection and/or injury, with increase in pressure inside the lumen due to obstruction and secretion, leads to the production of diverticula, and further action of these factors leads to inflammation and eventually perforation.

3. An especially high incidence of diverticulitis (74.4 per cent) occurs where the appendix has previously been ruptured.

4. Diverticulitis may run a rapid course to perforation and peritonitis. This can explain the known tendency for rapid progression in some cases of recurring appendicitis.

5. Perforative diverticulitis could explain the eccentric perforations encountered at operations.

INTRAPERITONEAL DRIP AFTER LAPAROTOMIES

Its Clinical Application

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AND
A. K. CARTON, M.D.
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THE RATIONALE and the experimental base on which intraperitoneal drip for postoperative administration of fluids is founded were presented in previous papers.[1] It was hoped that the customary methods of postoperative administration of fluids might be supplemented by the employment of intraperitoneal drip, if the following three rules were observed: (1) Instead of a rapid infusion, a slow drip is employed, (2) antibiotics are added for prophylactic purposes and (3) plastic tubing, without a needle, is used to exclude the danger of an injury of a vein.

Animal experimentation [1] has shown that intraperitoneal administration of dextrose, isotonic sodium chloride and vitamin solutions, but not amino acids, is well tolerated, that the fluid is promptly absorbed and that the drip does not contribute to a spread of a localized infection within the abdominal cavity.

One more phase of the problem remained to be investigated before a clinical trial was justified: Is there a danger of bacterial growth, formation of pyrogens or molds if the tubing remains in the peritoneal cavity a considerable period for the purpose of repeated administration of fluids?

To answer these questions, the following experiments were performed. A bottle, connected with plastic tubing (venopak [2]), was filled with fluid to be tested. After 48 or 66 hours the fluid was tested for sterility, pyrogens, molds and yeast. For bacteria a seven day incubation period and for molds and yeast a 15 day incubation period were observed before final readings were recorded. The following samples were tested: isotonic sodium chloride solution, 5 per cent dextrose in isotonic sodium chloride solution, 5 per cent dextrose in distilled water and 10 per cent vitamin solution in 10 per cent dextrose. The results showed that all samples passed the tests for bacteria, pyrogens, molds and yeast.[2] Thus, experiments in vivo and in vitro have substantiated the premises on which intraperitoneal drip is

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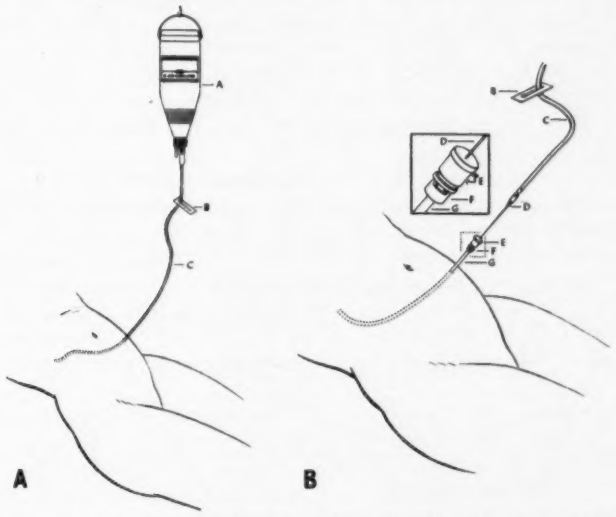
From the Department of Surgery, St. Elizabeth Hospital.

1. Narat, J. K.; Cipolla, A. F.; Cangelosi, J. P., and Vincenti, A. L.: Intraperitoneal Drip for Postoperative Administration of Fluids: Preliminary Report, Arch. Surg. **60**:102 (Jan.) 1950; Intraperitoneal Drip in Presence of Abdominal Infection: Experimental Study, Am. J. Surg. **79**:439 (March) 1950.

2. These experiments were performed at Abbott Laboratories, North Chicago, Ill., under the direction of Mr. H. C. Spruth. The plastic tubing venopak, the vitamin solution beclysyl® and all other solutions for the experiments and also for the clinical investigation were furnished by Abbott Laboratories.

based, have furnished proof that the method is innocuous and have justified its application in abdominal surgery.

The following simple technic has been developed for the clinical use of intraperitoneal drip. Shortly before or during the operation one of the circulating nurses unscrews the threaded cap from a 1 liter flask which meets the U. S. P. requirements for a type IV container for infusion solutions and adds 0.1 Gm. of streptomycin and 100,000 units of sodium salt of crystalline penicillin. Immediately before closure of the peritoneum the surgeon cuts off the rigid needle adapter with which the disposable tubing is usually equipped and inserts a segment of the tubing approximately 20 cm. long into the peritoneal cavity in such a manner that its end lies as far as possible from the incision and from the intra-abdominal organ operated on. For example, after an operation on the upper part of the abdomen the end of



A, set-up for continuous or uninterrupted intraperitoneal drip. *B*, set-up for interrupted intraperitoneal drip. *A*, fluid container; *B*, clamp; *C*, disposable tubing; *D*, 18 gage needle; *E*, rubber diaphragm; *F*, MacQuigg adapter; *G*, disposable tubing.

the tubing is placed into the pelvic cavity, whereas after a gynecologic operation the tip points toward the transverse colon. Peritoneum and fascia are closed snugly around the tubing to prevent leakage. After suturing of the skin the surgeon removes the protective covering from the dispensing cap of the tubing which protrudes from the wound and attaches the cap to the container held by the circulating nurse (fig., *A*).

The rate of the drip is regulated by the pinch clamp so that no more than 60 drops are delivered per minute. The fact must be kept in mind that not infrequently a change of position by the patient influences the rate of the flow and therefore frequent check-ups are desirable. To prevent leakage, the foot of the bed is raised after a surgical procedure on the lower part of the abdomen, and, conversely, the head of the bed is raised after an operation on the upper region of the

abdomen. When the container is empty, the tubing is withdrawn from the peritoneal cavity.

There is no problem of using several liters of solution in succession; all that is necessary is to unscrew the cap from the empty dispensing bottle and to attach it to a new container.

If solutions are to be given at certain intervals, two alternatives are at the disposal of the surgeon: 1. The procedure just outlined can be employed; in other words, the empty container remains attached to the tubing until it is replaced, when desired, by a new one. 2. If at the time of the operation it is planned to use more than 1 liter of solution, a short disposable unit (venotube or venoset [3]) is used, with the male and the female Luer adapters removed. The end of the tubing protruding from the incision is equipped with a "MacQuigg [4] adapter" which is covered with a rubber diaphragm (fig., *B*). The tubing attached to the fluid container is equipped with an 18 gage needle. The drip is started by piercing the aforementioned rubber diaphragm with this needle; when the fluid container is empty, the needle is withdrawn from the adapter. Whenever the drip is to be started again, the new dispensing bottle is connected with the tubing protruding from the abdomen, by piercing the adapter with the needle under sterile precautions.

The hydrostatic pressure of the fluid is apparently able to overcome the interference which may be created by the omentum or other intra-abdominal organs pushing against the outlet of the tubing within the peritoneum.

To demonstrate the rapidity of absorption of fluid from the peritoneal cavity, 10 cc. of a 5 per cent fluorescein solution was added to 1 liter of isotonic sodium chloride solution used for the drip. The dye was demonstrated in a blood sample taken from 8 to 10 minutes after the start of the drip. The experiment was performed on two patients, the Klett-Summerson photoelectric colorimeter being used.

Isotonic sodium chloride solution, or 5 per cent dextrose solution in distilled water or in saline solution respectively, with or without the addition of vitamins, was administered by intraperitoneal drip to patients at St. Elizabeth Hospital after various abdominal operations, namely, 1 gastroenterostomy, 4 cholecystectomies, 1 cholecystostomy, 1 exploratory laparotomy (retroperitoneal sarcoma), 5 appendectomies (3 acute, 2 chronic), 1 appendectomy, excision of ovarian cyst and supracervical hysterectomy, 1 excision of an ovarian intraligamentary tumor, 2 supracervical hysterectomies, 4 supracervical hysterectomies and salpingo-oophorectomies, 1 supracervical hysterectomy and anterior colporrhaphy and 2 panhysterectomies.

No untoward results that could be attributed to the intraperitoneal drip were noticed. Moderate leakage occurred in 3 cases in the early stages of the clinical application of the method. This leakage can be avoided by placing the tip of the tubing far away from the point where the latter emerges from the abdomen and by suturing the peritoneum snugly around it. Still better, the tubing may be brought out through a stab wound.

3. Both furnished by Abbott Laboratories.

4. Furnished by Mr. Oscar Schwidetzky, Director, Research Department, Becton, Dickinson and Company, Rutherford, N. J.

COMMENT

The number of patients in whom intraperitoneal drip was employed is not sufficient to be empirically conclusive, but the dearth of complications suggests that the method permits administration of fluids with impunity, providing strict asepsis is observed. Great stress is laid on the rate of flow. If the fluid is administered more rapidly than at the rate of 200 cc. per hour or 60 drops per minute, a transient distention of the abdomen may result. Ascites, acute or chronic peritonitis and carcinomatosis of the abdominal cavity may be considered contraindications to the use of the method.

For the treatment of shock the intraperitoneal drip would be inadequate because the absorption is too slow. Other methods, such as intra-arterial infusion, or venoclysis under pressure, effect a more rapid restoration of such vital factors as blood volume, blood pressure and oxygen-carrying power. This effect could be sustained, if necessary, over a longer period by the slower-acting intraperitoneal drip.

The next and, from the clinical point of view, probably the most important chapter of the study of intraperitoneal drip will deal with administration of blood. The intraperitoneal route as a means of transfusion has been studied by several investigators.[5] It is hoped that the superiority of the drip method over rapid infusion, in regard to better tolerance, absence of abdominal distention and avoidance of reaction, will apply not only to dextrose or saline solutions but also to blood.

CONCLUSIONS

1. Administration of dextrose or isotonic sodium chloride solution, with or without vitamins, by intraperitoneal drip is well tolerated. Antibiotics are added for prophylactic purposes.

2. The fluid is promptly absorbed if the rate of flow does not exceed approximately 60 drops per minute or 200 cc. per hour.

3. From a limited experience on clinical material, the method appears to be a convenient way of maintaining or reestablishing the water and electrolyte balance in patients who have undergone laparotomy and may be used to replace or supplement venoclysis.

1200 North Ashland Avenue.

5. Siperstein, D. M., and Sansby, J. M.: Intraperitoneal Transfusion with Citrated Blood, Am. J. Dis. Child. **25**:107 (Feb.) 1923. Florey, H. W., and Witts, L. J.: Absorption of Blood from the Peritoneal Cavity, Lancet **1**:1323 (June) 1928. Snead, C. R.: Absorption of Blood from the Peritoneal Cavity, Arch. Surg. **56**:249 (Feb.) 1948. Samuelsen, G. S.; Griffin, G. E.; Muntwyler, E., and Seifter, S.: Absorption of Blood from the Peritoneal Cavity of the Dog, Am. J. Physiol. **153**:277 (May) 1948.

MACRODEX IN THE TREATMENT OF EXTENSIVE BURNS

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DESPITE differences in opinion regarding the mechanism leading to shock, it is now agreed that this condition should not be treated with solutions of crystalloids. The best prophylactic and therapeutic agents are considered to be blood and plasma. However, these have several disadvantages. The provision of large quantities is difficult and expensive, their administration is attended by inevitable delay and by the risk of untoward reaction and of the transmission of virus infection.

Early experimental and clinical experience showed that in the treatment of shock the maintenance of an adequate volume of blood in circulation and of oxygen transport at a sufficient level was of primary importance. The amount of blood in circulation is determined to a large extent by the nature of the colloids in plasma and especially by the purely physical properties of these colloids. In this respect, their biologic properties are of minor significance.[1]

As soon as this fact was learned, attempts were made to use foreign body colloids, several of which were found to have an excellent shock-relieving effect. However, it was also found that organic injury and other undesirable effects often followed the administration of these substances, mostly because they could not be excreted or broken down.[2] These colloids have been tested for their effect in traumatic, postoperative and hemorrhagic shock, but there do not seem to be many reports of their effect on shock from burns.

MACRODEX (DEXTRAN PH)

In 1943 Grönvall and Ingelman[3] suggested that macrodex (or dextran Ph, as it was first called) could be used in the treatment of shock. After clinical tests

From the surgical departments of Karolinska Sjukhuset (Head, Prof. J. Hellström) and Serafimerlasarettet (Head, Prof. J. P. Strömbäck).

1. Bayliss, W. M.: Methods of Raising a Low Arterial Pressure, Proc. Roy. Soc. Med. **89**:380, 1917; The Action of Gum-Acacia on the Circulation, J. Pharmacol. & Exper. Therap. **15**:29, 1920. Starling, E. H.: On the Absorption of Fluids from the Connective Tissue Spaces, J. Physiol. **19**:312, 1896.

2. Hueper, W. C.: Macromolecular Substances as Pathogenetic Agents, Arch. Path. **33**:26 (Feb.) 1942.

3. Grönwall, A., and Ingelman, B.: Några nya kolloidlösningar för infusionsändamål, Nord. med. **21**:247, 1944.

by Bohmansson, Rosenqvist, Thorsén and Wilander,[4] the preparation began to be used extensively in Sweden. Reports of its efficacy are now also forthcoming from the United States of America, England and several other countries. Approximately 75,000 injections have been given in different conditions, with highly favorable results and few ill effects. The frequency of unfavorable reactions, calculated from 25,000 transfusion units given in Sweden, is 0.2 per cent.[5]

Macrodex consists of 6 per cent dextran in a 0.9 per cent solution of sodium chloride. Dextran is a high molecular polysaccharide of glucose. In the dextran used for macrodex the long molecules of the original substance have been broken down by hydrolysis to sizes corresponding closely to those of the blood protein molecules. The viscosity, specific weight and colloid osmotic pressure of the solution are approximately the same as those of plasma. The preparation is practically free from nitrogen, is nonantigenic and nontoxic. Apparently it can be entirely eliminated. It does not cause any local reaction or organic injury. In other words, it has none of the disadvantages of the earlier foreign body macromolecular colloids.[2] Moreover, in its present form it does not cause a clinically significant amount of erythrocytic aggregation, another unfavorable consequence of its predecessors.[6]

The administration of macrodex lowers the concentration of the plasma protein by dilution and also, it appears, by supplanting other proteins, the albumin fraction in particular.[7] Even the largest dose used for therapeutic purposes, however, does not lower the plasma protein concentration to a degree sufficient to affect the coagulability of the blood, wound healing, resistance to infection or formation of immune bodies.[5]

The supplanting of the albumin fraction seems to be part of a mechanism preventing the development of colloid osmotic hypertension. Most of the dextran molecules remain in the blood stream and maintain the intravascular colloid osmotic pressure. Their great attraction for water helps to maintain a large volume of plasma in circulation and causes the absorption of edematous fluid from the tissues, thereby eliminating any tendency to hemoconcentration.

Macrodex does not supply any nitrogen or protein. This is not a serious disadvantage because intravenously administered protein is apparently mainly used for the provision of calories and less for tissue formation or replacement of losses. The main benefit of this form of protein administration lies in its temporary osmotic

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4. Bohmansson, G., and others: Clinical Experiences with Dextran as a Plasma Substitute, Acta chir. Scandinav. **94**:149, 1946.

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6. Ivy, A. C., and others: The Effect of Various Blood Substitutes in the Resuscitation After an Otherwise Fatal Hemorrhage, Surg., Gynec. & Obst. **76**:85, 1943. Thorsén, H. G. R., and Hint, H. C.: Aggregation, Sedimentation and Sludging of Erythrocytes, Acta chir. Scandinav., 1950, supp. 154.

7. Malmros, H., and Thorsén, H. G. R.: Hur reguleras plasmaäggvitan? to be published Thorsén, H. G. R.: Dextran as a Plasma Substitute, Lancet **256**:132, 1949.

effect.[8] The intestinal route therefore remains the best means of replacement of lost tissue protein, and this route is nearly always available in burned patients.

PRINCIPLES OF TREATMENT

The burned surface and surrounding skin were cleaned with a 5 per cent soap solution or with detergent and bactericidal substances (invert soaps). Usually general anesthesia was not employed. Detached epidermis was carefully removed, and the raw surfaces were covered with a nonadherent pressure dressing. Tanning was not used. The primary dressing was not changed for 10 to 14 days. Penicillin was administered systemically. Copious quantities of fluid and of concentrated protein and other food were given by mouth.

Treatment to prevent and mitigate shock was begun as soon as possible before the local treatment and was continued until the edema was absorbed and clinical and hematologic examinations showed that the losses in plasma were restored. This generally took between one and a half and four days. The amount of fluid injected varied according to the size of the area involved; the latter was calculated by the method suggested by Berkow.[9] When the burn involved 20 to 30 per cent of the body surface, about 4 to 6 liters was generally given to adults during the first 36 to 48 hours. When the lesion covered more than 30 per cent, 8 to 10 liters was given during the first 48 to 60 hours.

In spite of the administration of such large amounts of fluid, signs of overhydration, e. g., pulmonary edema, were never seen. The course of the shock and the effect of treatment were followed by frequent examinations of the blood pressure, hemoglobin, blood count or hematocrit value and urinary output. The nonprotein nitrogen, alkaline reserve, serum albumin, icteric index and similar conditions were generally measured in casual specimens daily or every other day.

CLINICAL OBSERVATIONS

At first macrodex was given alternately with blood and plasma. Rosenqvist[10] reported the results of this form of treatment in 1947. He showed that macrodex had as good a therapeutic effect as plasma and did not carry the same risk of

8. Ashworth, C. T., and others: The Effect of Crystalloidal and Protein-Containing Solutions on the Body Fluids and Circulating Plasma Proteins, Am. J. Physiol. **140**:589, 1944. Bailey, O. T., and Hawn, C. V.: Effect of Crystallized Bovine Albumin on Tissues of Normal Animals: Morphologic Changes in Normal Rabbits Induced by Intravenous Injection of Crystallized Bovine Serum Albumin, Am. J. Path. **19**:267, 1943. Janeway, C. A., and others: Concentrated Human Serum and Albumin: Albumin in Treatment of Shock; Safety of Albumin; Albumin in Treatment of Hypoproteinemia, J. Clin. Investigation **23**:465, 1944. Kremen, A. J., and others: Studies on the Intravenous Administration of Whole Bovine Plasma and Serum of Man, Surgery **11**:333, 1942. Metcalf, W.: The Fate and Effects of Transfused Serum or Plasma in Normal Dogs, J. Clin. Investigation **23**:403, 1944. Nissler, K.: Über die parenterale Verwendung von menschlichem Serum, Klin. Wchnschr. **21**:1075, 1942. Taylor, F. H. L., and others: Preservation of Normal Human Plasma in the Liquid State: Comparative in Vitro Studies on Physiologic Activity of Labile Constituents of Liquid and Frozen Plasma, J. Clin. Investigation **23**:351, 1944.

9. Berkow, S. G.: A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, Arch. Surg. **8**:138 (Jan.) 1924.

10. Rosenqvist, H.: The Primary Treatment of Extensive Burns: Clinical Study, Acta chir. Scandinav. (supp. 124) **95**:1, 1947.

reactions and virus infection. Since his report, therefore, we have not used plasma but as a routine have given macrodex and whole blood alternately. The usual practice has been to give 1,000 cc. of macrodex alternating with 450 cc. of

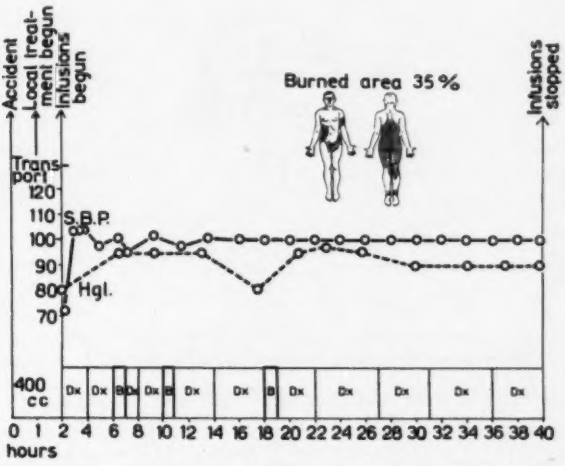

Fig. 1 (case 1).—The two curves in this figure (of a boy aged 2) and in figures 2, 3 and 4 represent the systolic blood pressure and the hemoglobin in per cent. The kind of substitutional fluid administered is shown in the rectangles, each of which represents 400 cc. The wider the rectangle, the more slowly the infusion was done. *Dx* signifies macrodex, *B* citrated blood, *S* saline solution, *Bi* sodium bicarbonate, *A* amino acids and *G* glucose, in this and the following charts.

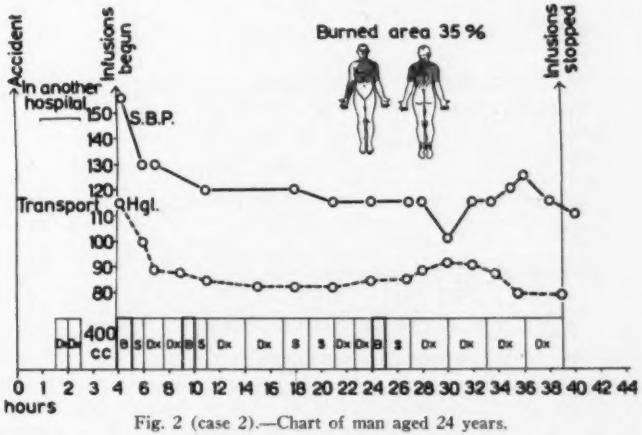

Fig. 2 (case 2).—Chart of man aged 24 years.

citrated blood. As several blood transfusions of this size were given during the course of the burn shock, they often were followed by a rise in the hemoglobin content, but this rise was counteracted by the next injection of macrodex. Crystalloid solutions have been used only occasionally.

A typical example of this form of antishock treatment is seen in case 1.

Case 1.—A boy aged 2, after 2 hours' transport and local treatment, was given altogether 3,800 cc. of macrodex, 1,050 cc. of citrated blood and 400 cc. of saline solution over a period of 42 hours. There was no fall in the blood pressure. He was discharged on the sixty-fourth day.

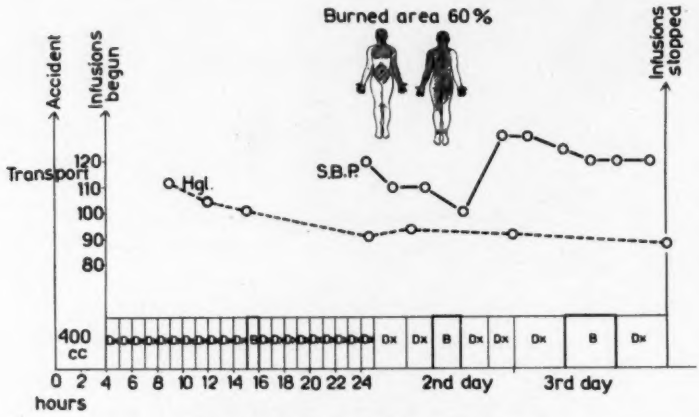

Fig. 3 (case 3).—Chart of man aged 45 years.

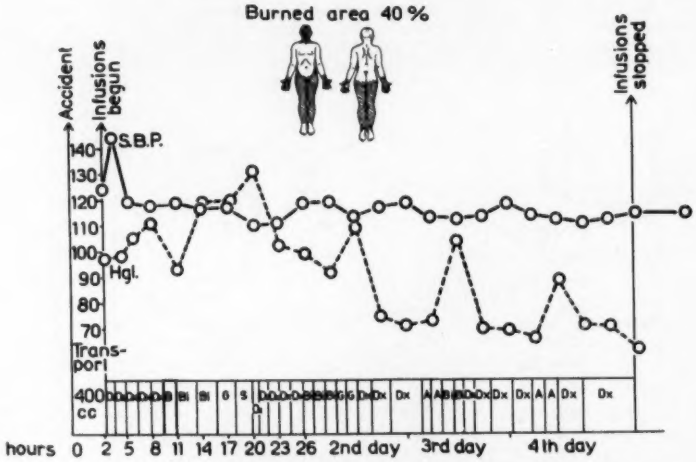

Fig. 4 (case 4).—Chart of man aged 22 years.

Macrodex is extremely useful in that it requires no great apparatus for its administration in patients before a long journey to a hospital. This is exemplified by case 2.

Case 2.—A man aged 24 was unconscious for 20 minutes after an electric burn. Before he was transported 40 Km. (24 miles) to the hospital, 800 cc. of macrodex was given. All in all,

5,600 cc. of macrodex, 1,050 cc. of whole blood and 2,300 cc. of electrolytes were given in the space of 46 hours.

One patient with extensive burns was treated almost exclusively with macrodex, with excellent results. The patient belongs to the group with the largest burned area who have yet been saved in Sweden.

CASE 3.—The patient was a man aged 45. Antishock treatment was begun after four hours' transport to the hospital. Altogether, 10,050 cc of macrodex and 1,200 cc. of whole blood were given during the course of 66 hours. There was no drop in blood pressure and no hemoconcentration. Blood tests at the end of the treatment showed carbon dioxide 58 volumes per cent, serum protein, 5.8 Gm. per 100 cc. (falling drop method), nonprotein nitrogen 35 mg. per 100 cc. of blood, chlorides 256 mg. and sodium chloride 472 mg. per 100 cc. of plasma. The patient was discharged after 105 days.

Results in Eleven Patients Treated with Macrodex

Source of Burn	Amount of Body Surface Burned, %	Sex, Age	Substitution Therapy			Infusion Time in Hours	Amount of Fluid Taken by Mouth, Cc.	Comment
			Macrodex, Cc.	Blood, Cc.	Crystalloids, Cc.			
Fire	20	♀ 75	4,800	1,050	None	36	4,400	Died after 17 days; pronounced aortitis; arteriosclerosis
Scalds	20	♂ 5	2,800	350	None	44	1,750	Survived; healed in 5 mo.
Fire	22	♂ 26	2,400	350	1,000	30	2,350	Survived; healed in 3 mo.
Fire	23	♂ 50	4,100	1,600	None	48	2,350	Survived; healed in 4 mo.
Scalds	24	♂ 3	2,400	700	600	43	1,850	Survived; healed in 3 mo.
Scalds	35	♂ 2	3,800	1,050	400	42	2,600	Survived; healed in 2.5 mo.
Electricity	35	♂ 24	5,600	1,050	2,300	46	Unknown	Survived; healed in 1.5 mo.
Fire	40	♂ 25	7,600	350	6,000	90	Unknown	Survived; healed in 4 mo.
Fire	42	♂ 47	9,500	1,050	2,950	44	Unknown	Died after 19 days from bronchopneumonia and septic pyelonephritis
Electricity	45	♂ 41	11,600	900	None	48	Unknown	Died after 5 days from sequelae of abdominal trauma and fracture of the skull
Explosion of aluminum powder	60	♂ 45	10,050	1,200	None	66	6,250	Survived; healed in 3.5 mo.

In case 4 macrodex was given alternately with large amounts of crystalloid solutions. It can be seen from the curve how macrodex given during shock rapidly eliminates the hemoconcentration and how infusion of substances without a colloid osmotic effect have an opposite effect.

CASE 4.—The patient was a man aged 25. Antishock treatment was begun two hours after he was burned. Altogether 7,600 cc. of macrodex, 350 cc. of blood and 6,000 cc. of crystalloids were given in the course of 90 hours.

SUMMARY OF CLINICAL FINDINGS

Our series of burn patients consists of all those, 11 in number, entering Karolinska Sjukhuset and Serafimerlasarettet during recent years with a second or third degree burn involving more than 20 per cent of the body surface. The size of the burned area was estimated at the first change of dressings. Only one case of a moribund 45 year old man, who got no treatment, is excluded. The lower limit in this series was set at 20 per cent because the general experience is that burns above this limit present a therapeutic problem, often with an unfavorable outcome, unless

they are properly treated. No death occurred among the patients with less than a 20 per cent burn treated in our hospitals within the same period.

The accompanying table gives the data on the 11 patients whom we treated. All were in remarkably good condition during the shock phase. In no case was there a fall in the blood pressure, and satisfactory amounts of urine were excreted. Three of the patients died, but these deaths were not connected with shock or the injections of macrodex. The causes of death are briefly stated in the table.

The specific gravity of the urine rose considerably when macrodex was given, values up to 1.060 being sometimes observed. This was due to the excretion of low molecular dextran in the urine, where its concentration might reach as high as 7 per cent. Low molecular dextran does not, however, leave the blood only by way of the kidneys; the contents of blisters from burns have been found to contain 0.5 per cent dextran.

As already mentioned, administration of macrodex caused a large drop in the plasma protein. Protein concentrations as low as 2.5 Gm. per 100 cc. were observed in some of our cases. Because of the colloid osmotic activity of the dextran the absorption of edematous fluid was unaffected by this reduction in plasma protein concentration.

We may mention that the concentration of plasma protein can only be determined gravimetrically or according to Kjeldahl's method. However, methods based on the specific weight of the plasma give a sufficient idea for clinical purposes of the combined effect of the plasma protein and dextran. A solution of 1.0 per cent dextran has the same specific weight as a solution of 1.3 per cent plasma protein.

As the concentration of dextran in the plasma begins to decline when the treatment is stopped, the concentration of plasma protein begins to rise. No other noteworthy changes were noted in the laboratory studies.

COMMENT

The most essential measures in the treatment of extensive burns are those to counteract shock and infection. We have used macrodex for the first of these purposes, with favorable results in every case as far as the shock is concerned. The three deaths were related to other factors. The results, therefore, are comparable with the best obtained with blood and plasma. Our cases are few, but they justify further work along the same lines. Macrodex has proved to be as good as plasma in preventing and reducing hemoconcentration and in maintaining the blood pressure and circulation. None of the usual objections to artificial colloid transfusion agents seems to apply to macrodex.

Provided that a sufficient quantity of protein for metabolization and replacement of losses can be administered by mouth, therefore, macrodex seems to be just as useful for treating shock from burns as plasma.

From a practical standpoint, macrodex is superior to plasma. It does not require the organization of donor corps and plasma banks. It does not incur a risk of a virus infection and is attended by a low frequency of complications on the whole. It involves no storage problems. It can be made accessible everywhere in unlimited

amounts. Finally, it is not expensive. Macrodex should be of great help particularly in small hospitals without large reserves of plasma, and in our opinion it will prove to be invaluable in case of war or other major catastrophes.

SUMMARY AND CONCLUSIONS

Eleven patients with burns of second and third degree involving between 20 and 60 per cent of the body surface were treated for shock mainly with the Swedish preparation macrodex. Every case responded favorably as far as shock was concerned. Three patients died of complications which had nothing to do with shock or the treatment with macrodex. Macrodex seems to be as good as plasma for the treatment of shock from burns and should therefore be of great aid, particularly in small hospitals and in times of war and other catastrophes.

MULTIPLE DIVISIONS OF THE RECURRENT LARYNGEAL NERVE

An Anatomic Study

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INJURY to the recurrent laryngeal nerve is one of the chief hazards of thyroid surgery. An accurate, anatomic knowledge of the course and variations of this nerve is essential if vocal cord palsy is to be avoided. Berlin [1] has stated that it is "the variability rather than the vulnerability" of this nerve which is responsible for the frequency of serious injury.

Clinical improvement in vocal cord paralysis following electrical stimulation therapy [2] led Weeks and Hinton [3] to the hypothesis that many nerves had extralaryngeal divisions and that the nerve supply to the laryngeal muscles on the affected side was frequently not completely interrupted but rather so reduced by the division of one branch that only when assisted by artificial stimulation could it regain motor control over the injured muscles. To explore this possibility, these investigators dissected 28 cadavers and found that 78 per cent, or 43, of the dissected recurrent laryngeal nerves divided extralaryngeally. The present anatomic study was undertaken to broaden the basis of these observations.

MATERIALS AND METHODS

One hundred recurrent laryngeal nerves in 50 cadavers were dissected. The usual thyroid approach was used. The pretracheal muscles were divided to facilitate exposure. The nerve was identified about 3 cm. above its origin as it approached the tracheoesophageal groove. The following data were recorded during each dissection. Was the nerve single throughout its course? If not, the point of division and number of extralaryngeal branches were noted. The relation of the nerve and any of its branches to the inferior thyroid artery and the relation of the upper third of the nerve to the thyroid gland and the posterior capsule were determined.

The dissections were painstakingly performed to insure that the extralaryngeal divisions were actually branches of the recurrent laryngeal nerve going to the

From the Department of Surgery of New York University Post-Graduate Medical School.

1. Berlin, D. D.: The Recurrent Laryngeal Nerves in Total Ablation of the Normal Thyroid Gland: Anatomical and Surgical Study, Surg., Gynec. & Obst. **60**:19-26 (Jan.) 1935.

2. Laszlo, A. F., and Fiertz, C. O.: Prognosis of Recurrent Nerve Paralysis Following Thyroidectomy, Arch. Otolaryng. **42**:372-373 (Nov.-Dec.) 1945.

3. Weeks, C., and Hinton, J. W.: Extralaryngeal Division of the Recurrent Laryngeal Nerve: Its Significance in Vocal Cord Paralysis, Ann. Surg. **116**:251-258 (Aug.) 1942.

larynx. Fibers of the recurrent laryngeal nerve to the trachea and esophagus are excluded from this study.

RESULTS

Of the 100 nerves dissected, 73 per cent divided extralaryngeally; 27 per cent persisted as single nerve trunks until they became intralaryngeal. Of the multiple extralaryngeal divisions, 37 (51 per cent) occurred on the right and 36 (49 per cent) on the left side (table 1).

The point of division in 45 (62 per cent) of the 73 nerves which showed multiple branches was at the junction of the middle and lower thirds of the thyroid gland (table 1; figs. 1, 2 *A*, 2 *B*, 2 *C*). Twenty-eight (38 per cent) showed terminal divisions posterior to the upper third of the gland, 0.5 to 1 cm. inferior to the point where the nerve becomes intralaryngeal.

TABLE 1.—*Variations of Recurrent Laryngeal Nerves*

Number of neck dissections	50		
Number of nerves	100		
Number of single nerve trunks			
Right side		13	
Left side		14	
Total			27
Number of multiple nerve trunks			
Right side		37	
Left side		36	
Total			73
			100
Number dividing in area of inferior thyroid artery		45 (62%)	
Number dividing posterior to upper third of gland		28 (38%)	
Total		73 (100%)	
Two branches		48 (66%)	
Three branches		19 (26%)	
Four branches		5 (7%)	
Five branches		1 (1%)	
Total		73 (100%)	

Of 73 nerves, 48 (66 per cent) divided into two divisions of approximately equal caliber (fig. 1 and fig. 3 *H*). Nineteen (26 per cent) showed three branches (figs. 2 *A*, 2 *B*, 2 *C*, 3 *F*), five showed four (fig. 3 *E*) and one nerve in this series divided into a major network of five extralaryngeal divisions (fig. 3 *G*). The caliber of these multiple divisions varied considerably. The usual arrangement was for the parent trunk to divide into branches of equal size. However, arrangements of 65 to 35 per cent, 50 to 25 to 25 per cent and 60 to 20 to 20 per cent were not uncommon.

Thirty four (34 per cent) of the nerves passed anterior to the inferior thyroid artery, 20 of these being on the right side and 14 on the left (figs. 1, 3 *F*). Forty-three (43 per cent) passed posterior to the vessel (figs. 2 *A*, 2 *D*, 3 *E*, 3 *H*), 16 on the right side and 27 on the left. In 23 (23 per cent) instances the nerve and its branches could best be described as being intermingled with the branches of the inferior thyroid artery (fig. 2 *B*, 3 *G*). This occurred 14 times on the right side and nine times on the left (table 2).

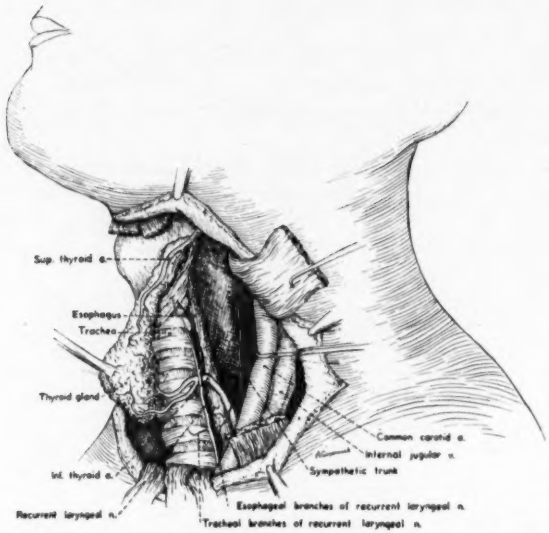

Fig. 1.—Typical anatomic relationships of the left recurrent laryngeal nerve.

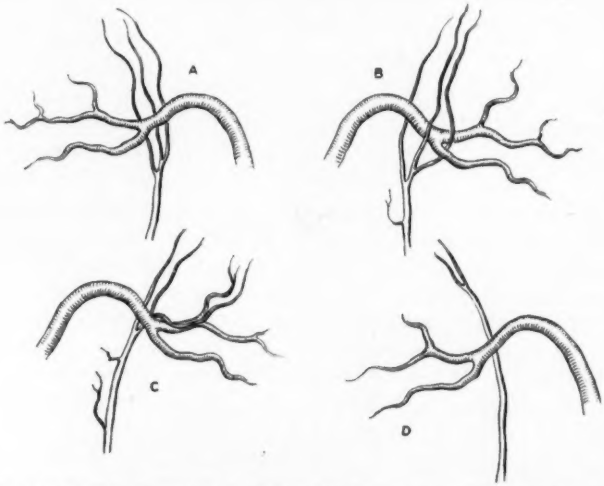

Fig. 2.—Variations in the anatomic relationships of the recurrent laryngeal nerve and the inferior thyroid artery. *A* and *D*, right side of neck; *B* and *C*, left side of neck.

In 20 of the dissections (40 nerves), the position of the upper one third of the nerve in relation to the thyroid gland was determined. Six nerves (15 per cent)

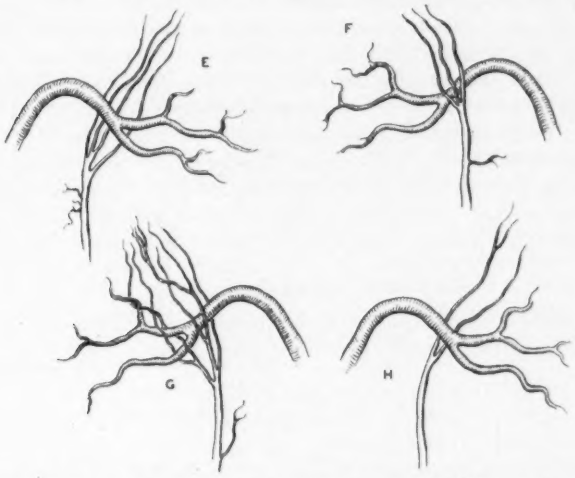

Fig. 3.—Variations in the anatomic relationships of the recurrent laryngeal nerve and the inferior thyroid artery. *E* and *H*, right side of neck; *F* and *G*, left side of neck.

TABLE 2.—*Position of the Nerve in Relation to the Inferior Thyroid Artery*

Position in Relation to Artery	No. of Nerves	Total
Anterior to artery		
Right side	20	
Left side	14	
		34
Posterior to artery		
Right side	16	
Left side	27	
		43
Intermingled with branches of artery		
Right side	14	
Left side	9	
		23
		100

TABLE 3.—*Position of the Recurrent Laryngeal Nerve in Relation to the Thyroid Gland in the Upper One Third of Its Course*

Position of the Nerve	No. of Nerves	Per Cent
Partially penetrated thyroid gland	6	15
Traverse adherent zone	10	25
Tracheoesophageal sulcus	24	60
	40	100

partially penetrated the substance of the thyroid gland for a distance of 0.5 to 1 cm. before becoming intralaryngeal, and one of these accompanied one of the terminal

twigs of the ascending branch of the inferior thyroid artery (fig. 2 *C*). Ten nerves (25 per cent) traversed the adherent zone, while 24 (60 per cent) occupied the classical position in the tracheoesophageal sulcus (table 3).

Two anomalies of the inferior thyroid artery were demonstrated. In the first, the inferior thyroid artery arose from the left common carotid artery and passed directly across to the thyroid gland (fig. 4 *I*). The nerve in this instance passed anterior to one branch of the artery and then divided to embrace another branch of the artery. In the other case, no inferior thyroid artery was present. In its place, a large branch of the superior thyroid artery descended on the posterolateral surface of the gland (fig. 4 *J*). A single nerve trunk ascended in the tracheoesophageal groove posterior to the vessel. According to Crile,[4] anomalies of origin, position and course of the inferior thyroid artery occur in about 6 per cent of the cases.

COMMENT

The course of the recurrent laryngeal nerve differs in the two sides of the neck. The two nerves arise from the vagus in the superior part of the thorax. The right

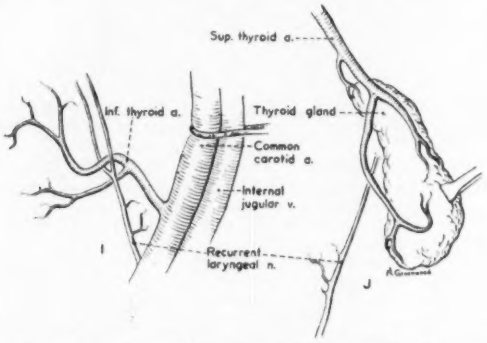

Fig. 4.—Two anomalies of the inferior thyroid artery. *I*, inferior thyroid artery arises from left common carotid artery; *J*, absence of right inferior thyroid artery (branch from superior thyroid artery replaces it).

passes from before backward around the right subclavian artery. The left hooks around the arch of the aorta. The left recurrent nerve more quickly reaches the tracheoesophageal sulcus, ascends more vertically and lies generally more posterior or deeper in the sulcus than the right recurrent nerve. Both nerves enter the larynx at the cricothyroid articulation through the fibers of the inferior constrictor muscles of the pharynx.

The distribution of these nerves to the laryngeal musculature is still a subject of controversy. It is a well accepted fact that the cricothyroid muscle is supplied by the external laryngeal branch of the superior laryngeal nerve and that the crico-arytenoid posterior (the abductor muscle) is supplied by the recurrent laryngeal nerve. The difference of opinion exists in regard to the innervation of the inter-

4. Crile, G., Jr., and Shively, F. L., Jr.: The Importance of the Inferior Thyroid Artery in Technic of Thyroid Surgery, S. Clin. North American **21**:1275-1289 (Oct.) 1941.

arytenoid muscle (the adductor of the vocal cord). Lemere [5] and Jackson [6] believe that the superior laryngeal nerve is entirely sensory to the mucosa of the larynx except for its external branch to the cricothyroid muscle and that the interarytenoid is supplied entirely by the reccurent laryngeal nerve (this muscle is a midline structure and as such received branches from both recurrent nerves). This conception is the classical anatomic one. Frazier [7] believes that the interarytenoid is supplied by motor branches from the internal division of the superior laryngeal nerve. Nordland,[8] in 19 laryngeal dissections, found the arytenoid supplied by the superior laryngeal nerve through its internal branch in 18 specimens, and in one specimen a branch of the recurrent and the internal branch of the superior laryngeal nerve supplied the muscle.

The clinical background for this argument lies in the fact that many cases of vocal cord palsy after thyroidectomy show the preferential abductor type of paralysis. It has even been postulated that the abductor fibers in the nerve were more sensitive to trauma than the adductor fibers and that the abductor fibers lay more external in the nerve and thus were more exposed to injury. Neither of these theories has been substantiated by scientific investigation.

On the basis of the present study, in which it has been shown that 73 per cent of the recurrent laryngeal nerves divide extralaryngeally, a different possible explanation for this phenomenon can be offered. Abductor paralysis following injury to the recurrent nerve is the commoner because of the bilateral innervation of the adductor muscle. Adductor paralysis would occur in spite of the bilateral innervation if one assumes that the recurrent nerve branched extralaryngeally and the branches injured carried only, or principally, adductor fibers. This situation would strike a balance greatly in favor of the abductor muscle, thereby giving the cord the appearance of an adductor paralysis.

The anatomic distribution of the recurrent nerve with extralaryngeal divisions would also explain the good clinical results obtained with electrical therapy. After the injury or division of one of the branches, the remaining branches could be stimulated to regain motor control over the laryngeal musculature. Division of all the branches or of a single nerve would result in failure of response to electrical stimulation.

There are recorded in the literature data on the extralaryngeal branches of the recurrent nerve. Berlin [1] reported two instances in 70 total thyroidectomies. Nordland,[8] in 31 cadavers, found six recurrent nerves with divisions. Lahey [9] states that he has repeatedly seen this extralaryngeal division of the nerve in the course of

5. Lemere, F.: Innervation of Larynx: Experimental Paralysis of Laryngeal Nerve, Arch. Otolaryng. **18**:413-424 (Oct.) 1933.

6. Jackson, C., and Coates, G. M.: The Nose, Throat, and Ear and Their Diseases, Philadelphia, W. B. Saunders Company, 1929, p. 763.

7. Frazier, C. H., and Erb, W.: The Superior Laryngeal Nerve and Superior Pole in Thyroidectomies, Ann. Surg. **101**:1353-1357 (June) 1935.

8. Nordland, M.: The Larynx as Related to Surgery of the Thyroid Based on Anatomical Study, Surg., Gynec. & Obst. **51**:449-459 (Oct.) 1930.

9. Lahey, F. H.: Operative Injury to the Recurrent Laryngeal Nerve, S. Clin. North America **12**:839-848 (June) 1932. Lahey, F. H., and Hoover, W. B.: Injuries to Recurrent Laryngeal Nerve in Thyroid Operations: Their Management and Avoidance, Ann. Surg. **108**: 545-562 (Oct.) 1938.

dissecting the nerve during thyroidectomies. Reed [10] found that 5.4 per cent of 506 dissected nerves divided into two or more branches while in direct relation to the inferior thyroid artery or its branches.

The relationship of the recurrent laryngeal nerve to the inferior thyroid artery, of great significance in thyroid surgery, has been the subject of much interest and investigation.

Berlin and Lahey,[11] after bilateral neck dissections in 22 cadavers, concluded that on the right side the nerve was oftener anterior to the artery (18 of 22), while on the left it was oftener posterior (19 of 22). However, Berlin,[1] after the dissection of 70 more cadavers, stated later that the nerve may be either anterior or posterior to the artery. Fowler and Hanson [12] found the nerve posterior to the artery in 65.5 per cent of 262 dissections, anterior to the artery in 26 per cent and intermingled with branches of the artery in 8.5 per cent. In Bachhuber's [13] series of 100 dissections, the nerve was posterior to the artery in 18 per cent on the right and in 11 per cent on the left, passed through the branches of the artery in 48 per cent on the right and in 33 per cent on the left and, on both sides of the neck, divided to embrace the artery in one case. Nordland's[8] dissections clearly indicated that there are no definite differences in the relations between the inferior thyroid artery and the recurrent laryngeal nerves on the right and left sides of the neck. This study confirms his observations.

Fowler and Hanson [12] were the first to show by anatomic dissection that the surgical capsule of the thyroid gland was difficult to demonstrate as a complete layer. This fascial envelop is well developed over the lateral surface of the thyroid cartilage, where it holds the superior pole of the gland firmly in place, but the major portion of what capsule is present does not ensheath the thyroid gland on its posterior and mesial surfaces, and here the recurrent laryngeal nerve lies against the gland itself. Blalock and Crowe [14] have indicated that most injuries to the nerve occur in this area.

Berlin [1] went one step further by describing how in this area 10 per cent of 140 dissected nerves partially penetrated or grooved the surface of the thyroid gland, 25 per cent traversed the adherent zone (which he describes as "an expression of normal anatomy indicating the fixation of the gland to the trachea just below the anterolateral aspect of the bar of the cricoid cartilage at the level of the first and second tracheal rings") and 65 per cent ascended in the tracheoesophageal sulcus, where the nerve is best protected from operative injury.

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10. Reed, A. F.: The Relations of the Inferior Laryngeal Nerve to the Inferior Thyroid Artery, Anat. Rec. **85**:17-23 (Jan.) 1943.

11. Berlin, D. D., and Lahey, F. H.: Dissections of Recurrent and Superior Laryngeal Nerves: Relation of Recurrent to Inferior Thyroid Artery and Relation of Superior to Abductor Paralysis, Surg., Gynec. & Obst. **49**:102-104 (July) 1929.

12. Fowler, C. H., and Hanson, W. A.: The Surgical Anatomy of the Thyroid Gland with Special Reference to Relations of Recurrent Laryngeal Nerve, Surg., Gynec. & Obst. **49**:59-65 (July) 1929.

13. Bachhuber, C. A.: Complications of Thyroid Surgery: The Anatomy of the Recurrent Laryngeal Nerve, Middle Thyroid Vein and Inferior Thyroid Artery, Am. J. Surg. **60**:96-100 (April) 1943.

14. Blalock, A., and Crowe, S. J.: The Recurrent Laryngeal Nerves in Dogs, Arch. Surg. **12**:95-116 (Jan.) 1926.

This present study is in complete agreement with Berlin's findings. Figure 2 *C* shows the close proximity of a branch of the recurrent laryngeal nerve to the ascending branch of the inferior thyroid artery in this "danger area," and this branch of the nerve grooved the posterior surface of the gland.

SUMMARY AND CONCLUSIONS

Seventy-three of 100 dissected recurrent laryngeal nerves divided extralaryngeally. This is consistent with the clinical phenomenon of preferential paralysis of the vocal cords and the good results obtained with electrical treatment in some cases of vocal cord palsy after thyroidectomy.

The most frequent point of division of the nerve is in relation to the inferior thyroid artery, but branching also occurs in the upper one third of the extralaryngeal course of the nerve.

The commonest number of divisions of the nerve was two, but instances of branching into three, four and five components were encountered.

The recurrent laryngeal nerve may pass anterior, posterior or through the branches of the inferior thyroid artery, and there are no definite differences in the relationship between the artery and the nerve on the right and left sides of the neck.

In the upper one third of its course, the recurrent nerve occupies a relatively safe position in the tracheoesophageal groove, but it may traverse the adherent zone and may even groove the posterior surface of the thyroid gland where the surgical capsule is deficient.

Two anomalies of the inferior thyroid artery are described.

USE OF VARIOUS PLASTIC CATHETERS IN THE SUBARACHNOID AND PERIDURAL SPACES

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THE FIRST continuous conduction nerve block anesthesia performed through an indwelling catheter was instituted by Eugene Aburel, of Rumania, in the clinic of Professor V. LeLorier and reported to the Society of Obstetrics and Gynecology in Paris in 1930.[1] Aburel inserted a 14 cm. needle to the left of the vertebral column just anterior to the lumboaortic nerve plexus. Through this needle he introduced a fine elastic silk catheter which remained in place after the withdrawal of the needle. Thus was developed the technic for serial or continuous aortic anesthesia.

In 1935 Love [2] reported the use of an indwelling ureteral catheter for continuous subarachnoid drainage for meningitis. He introduced a no. 4 or no. 5 French catheter through a 13 gage Barker needle. This technic was next utilized in the United States in 1941 by Manalan,[3] of the University of Indiana, for the introduction of an indwelling catheter into the sacral canal. Adams, Lundy and Seldon,[4] of the Mayo Clinic, modified continuous caudal analgesia in 1942 by the institution of the 13 gage needle through which a no. 5 ureteral catheter, woven silk or preferably nylon, was placed into the sacral canal as a preliminary to the withdrawal of the

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1. Aburel, E.: Bull. Soc. d'obst. et de gynéc. **19**:616, 1930.

2. Love, J. G.: Continuous Subarachnoid Drainage for Meningitis by Means of Ureteral Catheter, J. A. M. A. **104**:1595 (May 4) 1935.

3. Manalan, S. A.: J. Indiana M. A. **35**:564, 1942.

4. Adams, R. C.; Lundy, J. S., and Seldon, T. H.: Continuous Caudal Anesthesia or Analgesia: Consideration of Technic, Various Uses and Some Possible Dangers, J. A. M. A. **122**:152 (May 15) 1943.

needle. Irving,[5] of Syracuse, Brown,[6] of Cook County Hospital, and others greatly extended the use of this technic in the management of labor and delivery.

In 1944 Tuohy,[7] of Georgetown University, described the continuous spinal technic using an indwelling catheter, and in 1945 [8] he developed a Huber point type of needle through which the shellacked radiopaque special catheter was inserted in a directional route cephalad or caudad into the subarachnoid space.

We began the use of these technics a few months later. Simultaneously in March 1946 at the University of Tennessee in Memphis and at the Johns Hopkins Hospital, we substituted the polyethylene and the vinylite (B-D vinyl tubing) plastic catheters for the costlier, larger and more traumatic shellacked nylon ureteral catheters for the technics of continuous caudal, continuous peridural and continuous spinal analgesia and anesthesia. Since that time we utilized these technics in obstetrics, surgery and therapeutics in more than 1,900 cases.

The present study covers the use of these plastic catheters for the continuous administration of anesthetics and therapeutic medicaments in the Johns Hopkins

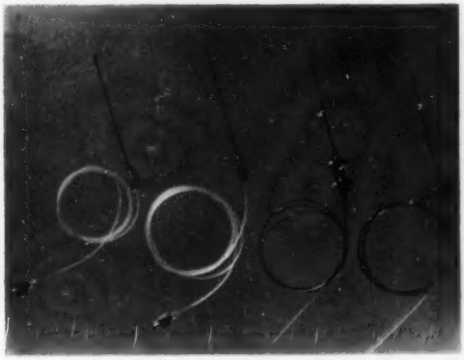

Fig. 1.—Four catheters and various needles.

Hospital and allied institutions from July 1, 1948 to June 1, 1950. We have used four types of catheters during this period: polyethylene, vinyl, radiopaque nylon ureteral and nonradiopaque ureteral.

The polyethylene catheter has been used in the majority of cases. Kirchof and Boals [9] found this tubing to be excellent for continuous spinal anesthesia, and we have found it equally efficacious for the other technics. The tubing is flexible and relatively inelastic but will stretch markedly without breaking. It is inexpensive, and it has been our policy to discard it after each use. It is easily introduced through

5. Irving, F. R.: Improvement in Catheter Technic for Continuous Caudal Anesthesia, J. A. M. A. **122**:1181 (Aug. 21) 1943.

6. Brown, H. O.; Thomason, J. M., and Fitzgerald, J. E.: Anesthesiology **7**:355, 1946.

7. Tuohy, E. B.: Anesthesiology **5**:142, 1944.

8. Tuohy, E. B.: Use of Continuous Spinal Anesthesia Utilizing Ureteral Catheter Technic, J. A. M. A. **128**:262 (May 26) 1945.

9. Kirchof, A. C., and Boals, D. C.: West. J. Surg. **57**:88, 1949.

a 17 gage needle and admits a 25 gage hypodermic needle. There are possibly two disadvantages to the polyethylene catheter. One lies in the fact that it must be prepared for use by chemical sterilization. The tubing is perfused with a solution of zephiran® chloride (1:1,000), then coiled and immersed in the same solution for 24 hours. This method of sterilization has been most satisfactory for us, and we have encountered no reactions that we could attribute to the method of sterilization. Occasionally some difficulty is encountered because of the flexibility of the polyethylene catheter. We have noted this occasionally in attempting to place the catheter into the peridural space through the Tuohy needle and have found it advisable to substitute the more rigid vinyl catheter or the ureteral catheter with the stilet in place.

The B-D vinyl tubing catheters have proved satisfactory, but until recently they have been available in only limited supply. This catheter is slightly less flexible than the polyethylene one and offers two distinct advantages. It may be sterilized by autoclaving and is of smaller diameter, but it has a larger lumen than the polyethylene tubing. It is easily introduced through an 18 gage needle and will

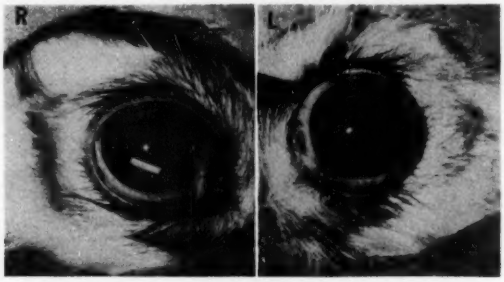

Fig. 2.—Catheter material inserted into rabbit's eye.

admit a 23 gage hypodermic needle. We have found it of particular value in the subarachnoid space, where repeated withdrawal of spinal fluid may be desired. We have used the vinyl catheters from two to ten times each without difficulty.

Occasionally we have used the no. 3.5 French shellacked nylon ureteral catheter. Its chief disadvantage lies in its expense, and we prefer the nonradiopaque catheter for routine use, as the cost is 50 per cent less. These catheters are sheathed in long test tubes with the stilet in place and sterilized by autoclaving. We have found them to be particularly valuable when difficulty is encountered in introducing a more flexible catheter into the peridural space through the Tuohy needle. The 3.5 ureteral catheter is introduced through a 16 gage needle and admits a 25 gage hypodermic needle.

Each batch of catheter material that we have obtained has been first tested for irritative properties by inserting a small segment of it into the anterior chamber of the rabbit's eye. This method places the material where it is easily observed and also in a sensitive medium. The rabbit is observed for seven days, and if there is no evidence of reaction at the end of that time the tubing is prepared for clinical use.

During the 23 months covered by this study plastic catheters were used in the subarachnoid and peridural spaces for the continuous administration of anesthetics

and therapeutic medicaments for a total of 1,913 times. The number of various technics is shown in tables 1 and 2.

We have found the use of the indwelling catheters most advantageous on a busy delivery floor. The catheter may be placed early in labor, taped in place and used later when analgesia and anesthesia are required. Frequently the catheter is placed in the sacral canal at the time of rupture of the membranes for induction of labor and used later when labor is well established. It also enables the anesthetist to meet operating schedules with ease. The catheter may be inserted early and a satisfactory level of anesthesia obtained in advance of the time of operation.

TABLE 1.—*Use of Plastic Catheters in Johns Hopkins Hospital*
July 1, 1948 to June 1, 1950

	Continuous Caudal	Continuous Spinal	Continuous Peridural		Total
For Anesthesia:					
In obstetrics	1,065	149	116		1,330
In surgery, gynecology and urology	30	44	21		95
In therapeutics					66
Control of pain, advanced malignant growths				5	
Control of postoperative pain				8	
Repeated intraspinal medication and spinal fluid analysis				7	
Treatment of thrombophlebitis and vascular occlusion				3	
Treatment of anuria				12	
For examination and operation in rectal disease				2	
Control of pain in vulvovaginitis				1	
Splanchnic block in acute pancreatitis				1	
Treatment of postspinal headache				25	
For cystoscopy in poor risk child				1	
For segment localization prior to alcohol injection				2	
				66	
Grand total					1,491

TABLE 2.—*Use of Plastic Catheters in Other Hospitals*

	Continuous Caudal	Continuous Spinal	Continuous Peridural
Sinai Hospital, Baltimore, July 1, 1949 to June 1, 1950	389	2	5
Catheter blocks for consultation management in other hospitals	10	11	7
	399	13	12

The plastic catheter is nonirritating and does not limit the patient's movement. By careful application of adhesive tape, we are able to maintain it in place for long periods. On the obstetric service we have left it in place several times for periods of three days. This has been done in order to control postoperative pain and occasionally to control the hypertension in eclampsia and severe preeclampsia.

We have also used the plastic catheter for the administration of peridural and subarachnoid injections of saline solution in the treatment of severe postspinal headache in 25 cases. This technic was reported by Rice and Dabbs [10] earlier this year. We have found a much wider field for use of these technics in their special application in surgery, medicine and pediatrics. In advanced malignant disease of the prostate the indwelling plastic catheter enables one to provide pain relief for prolonged periods when the patient has become resistant to the opiates. We have

10. Rice, G. G., and Dabbs, C. H.: Anesthesiology **11**:17, 1950.

used the catheter to administer local anesthetics for temporary relief, and when the involved segments have been localized we have injected alcohol through it to produce a permanent block. This technic was also used satisfactorily in the treatment of pelvic pain following irradiation for carcinoma of the cervix.

In the treatment of tuberculous meningitis the indwelling spinal catheter enables the physician to administer streptomycin repeatedly and to withdraw spinal fluid for analysis as often as needed without the necessity of repeated spinal punctures. In a child with tuberculous meningitis and associated tuberculosis of the spine, the indwelling spinal catheter offered a method for continuation of streptomycin therapy

Fig. 3.—Spinal cord without local reaction to continuous streptomycin therapy with catheter for nine days. Patient died with extension of tuberculous meningitis into optic chiasm.

after she was placed in a plaster cast. One patient with tuberculous meningitis had an indwelling subarachnoid spinal catheter for 142 days, and at autopsy there was no evidence of local reaction, either grossly or microscopically.

Two patients with severe pain from rectal fistulas could not tolerate the preliminary examinations. Indwelling caudal catheters provided anesthesia for examination, operation, and postoperative control of pain. In a patient with painful vulvovaginitis following a radium burn relief was provided for five days prior to vulvectomy through an indwelling caudal catheter, and it was noted that there was much less local induration during the block. In one patient with acute pancreatitis a catheter was inserted into the epidural space and advanced to the region of the

ninth thoracic vertebra and a splanchnic block maintained in an effort to relax the sphincter of Oddi. Our experience with local block in this condition has been limited to this one case, but others [11] have reported good results from splanchnic block in acute pancreatitis.

In using plastic catheters in the subarachnoid and peridural spaces in 1,915 cases and for periods from a few hours to 142 days, we have encountered complications in only two cases. In one patient cellulitis superficial to the sacrum developed after continuous caudal anesthesia. This responded rapidly to chemotherapy and local heat and left no sequelae.

The second patient was a 21 year old white woman who had a polyethylene catheter placed in the subarachnoid space prior to a sterile vaginal examination for possible placenta previa. No drug was ever administered through the catheter. Three hours after its insertion all the signs and symptoms of an acute and most severe meningitis developed. The spinal fluid cell count revealed 2,300 white blood cells, with 94 per cent polymorphonuclear cells. The patient was treated with massive doses of penicillin and was markedly improved in 24 hours. Repeated spinal fluid cultures failed to produce any growth, and we felt that the condition was an aseptic meningitis which followed the introduction of the polyethylene catheter. The patient was delivered two days later without difficulty and had no sequelae from the meningitis. A portion of the same batch of catheter tubing was tested in the anterior chamber of the rabbit's eye, and no reaction was noted.

SUMMARY AND CONCLUSIONS

Plastic catheters have been used by us or under our supervision as conduction anesthesia conduits in caudal, peridural and subarachnoid spaces in 1,915 cases by 59 administrators without serious accident or complications other than those reported herein.

The use of the catheter has removed the major objection to continuous nerve block anesthesia, namely, (*a*) the probability of trauma from indwelling needles of both malleable and stiff varieties, (*b*) the likelihood of withdrawal of the needle from the proper space, (*c*) the possibility of inadvertent spinal anesthesia due to secondary thecal needle puncture in a moving patient and (*d*) needle breakage. It permits patients undergoing anesthesia or therapy to lie comfortably in any position, to move when necessary and on occasion to be ambulatory about the ward. There has been no increase in a low, almost negligible incidence of infection. The catheter has assured a means of prolonged anesthesia which can be readily maintained by a nurse-physician team on a 24 hour basis. It offers special promise in the prolonged control of intractable pain and in continuous antibiotic therapy into any of the vertebral spaces.

This study supports the use of plastic tubing for needles in prolonged intravenous therapy and in exchange transfusions.

ABSTRACT OF DISCUSSION

DR. J. W. SHUMAN, JR., Los Angeles: The mechanical aspects of anesthesia offer a fertile field for investigation, always with the aim of making our work safer and more simple. The introduction of plastics into the field of subarachnoid and peridural anesthesia marks a definite

11. Gage, M., and Floyd, J. B.: Tr. South. S. A. **59**:415, 1949.

improvement over materials previously available for this purpose. This is true in many other fields, since these substances may be tailored to individual requirements. The use of polyethylene tubings for intravenous infusion, nasal introduction of oxygen, gastric lavage and endotracheal tubes makes it natural for these versatile synthetics to find a place with the regional anesthesiologist.

In considering the use of plastic materials for the purpose of continuous subarachnoid and peridural introduction, a number of questions come to mind. First, are these catheters inert in the tissues as well as to the solutions to which they are exposed? Polyethylene sheets have been used around tendon grafts and other tissue reconstructions with no apparent adverse tissue response. It would seem reasonable that in view of the precautions taken by the authors in preparing such tubing this hazard would be minimal, although allergic reactions cannot be ruled out. Information that has been presented by the commercial suppliers of intravenous equipment stress the safety of this tubing for all types of fluid therapy.

The methods of sterilization may pose another problem. Heat usually affects plastics adversely, although autoclaving is probably the safest means of sterilization. If the cost of these materials is sufficiently low, a single sterilization would eliminate the deterioration of repeated exposures to heat and, at the same time, simplify the cleansing and storage problem.

Mention of headaches after puncture raises the question of tube caliber. The cause of these headaches apparently is still obscure, although considerable focus has centered on the size of the dural tear. For peridural technics, the method would appear ideal, especially when prolonged autonomic block therapy is needed.

Finally, the method itself may require some justification other than the fact that it is possible to conduct a continuous nerve block using a plastic catheter. Such potentially lethal medication should require more than cursory supervision by the anesthesiologist. Yet as the hours pass, the economic aspects of this method become ever greater to the patient, perhaps even to the point where the anesthesiologist's fee could exceed that of the obstetrician or the surgeon. In teaching institutions or other facilities making use of less qualified professional persons, these methods may be practical. But in individual private practice, this technic must be restricted in its application unless a safe, less expensive means is found to supervise the periodic or continuous introduction of medications.

The means of peridural and subarachnoid medications proposed are a definite advance in our armamentarium, although the method is still limited for many of us.

DR. CHARLES C. WYCOFF: The limpness of the polyethylene catheter as well as the need for cold sterilization will limit its use considerably. It is an accepted view that routine autoclaving with steam establishes and maintains sterility far better than soaking in antiseptic solutions. The possibility of contamination is too great with the cold sterilization technic. An infection in the soft tissues is not good, but the possibility of meningitis is horrendous, particularly in suit-conscious California. When the vinethyl catheters become available, they should certainly replace the conventional shellacked nylon catheters.

The vinethyl catheter allows one to use an 18 gage needle for continuous spinal anesthesia. It is commonly agreed that the size of the needle determines, in part, the incidence of spinal headaches. The use of an 18 gage needle should produce fewer headaches than the use of a 16 gage needle, which is ordinarily used.

The authors' use of the catheter to cure spinal headaches is particularly interesting. We have done several repeat spinal punctures to alleviate the headaches. Our results have been good but not uniformly successful. We did find on reviewing the literature that it is well to use Ringer's solution for injection rather than saline. We found several patients becoming apprehensive and shaky when over 50 cc. of saline was injected intrathecally. We have used as much as 300 cc. of Ringer's solution intrathecally and had no reaction other than cure of headache.

It is a worth while idea to place the caudal catheter early in labor. Frequently caudal anesthesia is desired at an inopportune time. When a catheter has already been placed, a speedy anesthesia is assured. I assume the authors administer a test dose when the catheter is first placed. At times it is difficult to be certain that the catheter is in the caudal canal. The onset of anesthesia proves the correct placement of the catheter.

DR. ROBERT A. HINGSON, Baltimore: We agree with both the discussers that heat sterilization is preferred to chemical wet sterilization. However, now we are able to get vinethyl catheters in quantity. Our future use of this technic therefore will eliminate the objectionable feature of wet sterilization. We wish to point out that no major complication has developed from the use of either type of catheter.

The test dose is always used first, as Dr. Wycoff suggested, after the laying of the catheter, if we have laid it for an anesthetic. The possibility of a reaction is always borne in mind. We do not infer that 1,900 cases without reaction means that there will not be a rare patient sensitive to one of these plastics, but we certainly can say that most patients are relatively insensitive to the catheters.

The economics of anesthesia is not within the realm of the discussion of this paper. We have been developing new technics and spreading the scope of the injection technic for several years in this particular field of anesthesia. We certainly agree that the financial problem in some situations would make prolonged, continuous nerve blocks impossible. However, they do have their place in the control of pain and in the extending of the services of the anesthesiologist, not only to the surgeon but to the clinician and to the internist who has to treat patients for prolonged periods with intractable pain.

SIMPLE METHOD OF BONE GRAFTING FOR NONUNION OF THE TIBIA

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CHICAGO

THE INCIDENCE of nonunion in fractures of the lower third of the tibia is greater than that in fracture of any of the other long bones. Among the various etiologic factors responsible for this condition are (1) poor local blood supply of the bone and (2) a relative lack of muscular and fascial tissues, with coaptation of fractures in this site. Furthermore, nonunion in this site may follow an inadequate period of immobilization. Surgical procedures, with their concomitant trauma, manipulation and introduction of metal screws and plates, will further reduce the local blood supply of bone and soft tissues. Although operative intervention may in the majority of instances result in good union without infection, still, because of the poor local blood supply, a percentage of fractures in this region so treated will be followed by nonunion, often with osteomyelitis. The latter condition may be caused by operative infection or by an original compound wound.

Many methods have been described for the treatment of nonunion of the tibia. The usual operative procedure consists of the introduction of a metal plate or the use of single or dual bone grafts or both, in each case the material used being held firmly in place by screws. It is advised to expose, curet or drill the bony, nonunion ends and realine them. The fibula in many instances is osteotomized at the time of operation. In the event of local infection of soft tissue or bone the operative procedure is delayed for several months to years.

In 1923 Phemister [1] introduced the onlay bone graft without internal fixation, utilizing this method for a nonunion of the mandible. Recently, he [1] reported a series of cases in which he also used this method for nonunion of fractures of long bones, metatarsal bones and the pelvis. The present paper deals with the results obtained in our clinic with the use of this method for the treatment of nonunion of the lower third of the tibia.

SURGICAL TECHNIC

After proper preparation of the patient and the extremity involved, a long double-curved incision is made from a point below the tibial tubercle to a point above the tibioastragalar joint (fig. 1). The proximal portion of the curve is directed medially and the distal part directed laterally, the incision at the distal end

From the service of Dr. D. S. Miller, Cook County Hospital.

Read before the Section on Orthopedic Surgery at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

1. Phemister, D. B.: Treatment of Ununited Fractures by Onlay Bone Grafts Without Screw or Tie Fixation and Without Breaking Down of the Fibrous Union, J. Bone & Joint Surg. **29**:946-960 (Oct.) 1947.

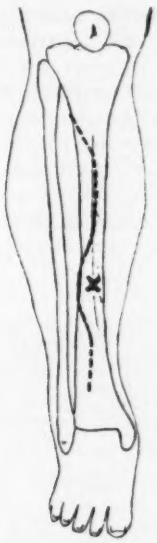

Fig. 1.—Drawing showing the type of operative incision used for the onlay bone graft operation.

Fig. 2.—Correct placement of onlay bone graft.

being made directly over the anterior tibial compartment. In this manner any existing operative scars over the tibia are avoided and more normal tissue which should heal readily is utilized.

Through the upper portion of the exposure a full thickness cortical bone graft about 4½ to 5 inches (12.7 cm.) long is removed from the proximal end of the tibia. The distal part of the incision affords access to the nonunion site and continues through healthy tissue to the lateral surface of the lower third of the tibia. This site is exposed subperiosteally, and bony excrescences, rough surfaces or soft tissue ossifications are removed, care being taken not to damage the anterior tibial vessels. After the periosteum has been carefully peeled from this site, the bone

TABLE 1.—*A Comparison of the Rigid Fixation Technic and of the Simple Onlay Method*

A. Rigid Fixation Method	B. Simple Onlay Method
1. Skin incision and subperiosteal exposure of nonunion in entire circumference	1. Skin incision and subperiosteal exposure of one surface of bone only
2. Complete removal of interposed fibrous tissue, baring nonunion bony ends	2. Leveling of recipient bony site is done only if necessary to provide flat surface
3. Medullary cavity is opened both proximally and distally	3. Bone graft is laid alongside the nonunion site without fixation. Closure
4. Bony sclerotic ends are resected to live vascular bone	4. Plaster of paris cast is applied
5. Bone ends approximated and fragments alined	
6. A bed for the graft is cut	
7. Bone graft is fitted to bed and/or screwed tightly to recipient bone or otherwise held. Closure	
8. Plaster of paris cast is applied	

TABLE 2.—*Summary*

Total number of cases observed	23
Number of males	17
Number of females	6
Previous operation	20
Adherent scar over nonunion	20
Duration of nonunion	8 mo. to 11 yr.
Time required for bony union following simple onlay graft	6 wk. to 5 mo.
Open ulcer healed after procedure	10
Open ulcer persisted	3
Successful unions	22
Failures	2

(One patient reoperated on and included in successful group above)

graft, flattened surgically, is placed between the cortical portion of the tibia and the anterior tibial compartment muscles (fig. 2). As a result, the medullary portion of the graft is in contact with the cortical side of the tibia. The wound is closed by interrupted sutures, and a circular well-fitting cast is applied from the groin to the toes.

RESULTS

Twenty-three patients with nonunion of the lower third of the tibia were treated by onlay bone graft without internal fixation. Before coming under our observation, many of these patients had been subjected to multiple operative procedures because of the persistence of nonunion (table 2). From the past operative history, the majority of them had been treated by the conventional surgical procedures (table 1 *A*), in contrast to the simple operative technic herein outlined (table 1 *B*).

The ages of the patients in this series varied from 15 to 67 years, with an average of 45 years. Seventeen were males and six were females. The duration of nonunion, before the present operation, varied from eight months to 11 years, with an average of 2.2 years. Seventeen patients had undergone one to four previous surgical procedures, while six had not been operated on before. Adherent scars, directly over the lower third of the tibia, were present in all but eight cases. Low grade, draining sinuses, due to infected sinus tracts, and low grade osteomyelitis or osteitis were present in 13 of the 23 cases.

In 22 cases bony healing occurred in from six to 21 weeks after operation. In the remaining patient (case 7) nonunion and osteomyelitis persisted and subsequent amputation was necessary. This patient had undergone four previous

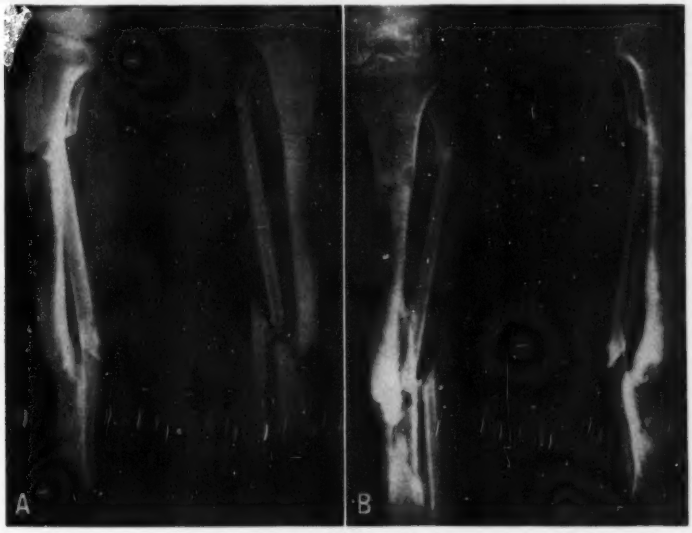

Fig. 3 (case 1).—*A*, nonunion of tibia and fibula with displacement of fracture fragments. *B*, onlay bone graft in situ. Bone healing has taken place at both ends (three months after operation).

operations in an attempt to treat the nonunion. It is of interest that amputation had been contemplated in three other cases but that in these healing had occurred after the onlay bone graft.

In all instances weight bearing was not allowed until bony union, as demonstrated clinically and on roentgenograms, was present. Roentgenologic studies were made every three to four weeks throughout the healing period.

A few typical cases are presented in order to illustrate surgical backgrounds and to demonstrate the rate of bone healing following the simple onlay bone graft.

CASE 1.—H. E., a woman aged 35 years, was injured in an automobile accident on Nov. 8, 1947, sustaining a compound fracture of the tibia and fibula (fig. 3). Skeletal traction was applied for a six week period. Because of the massive compound wound infection, surgical débridement was then done and a long leg cast applied. Two weeks after this procedure a sequestrectomy

was performed. Subsequently a skin graft was applied over the ulcerated area. The patient continued to have local drainage and was first seen by us in the orthopedic clinic 13 months after the original accident. There was roentgenographic evidence of nonunion of the tibia and fibula, with lateral displacement of the distal fragments. Marked sclerosis of the proximal tibial fragment was present. Culture of drainage revealed Escherichia coli. Penicillin and streptomycin were both administered, with a resulting afebrile reaction occurring approximately five days later. On Oct. 29, 1948, the patient was operated on; a simple onlay bone graft without internal fixation was used. A sequestrum was found and removed, and a small pocket of granulations that was encountered in the lateral aspect of the tibia was curetted. The bone graft was taken from the proximal tibia and snugly placed adjacent to the nonunion site. The wound was firmly closed, and a groin-to-toes cast was applied. Bony healing as evidenced by roentgenologic and clinical examination took place in four months and two weeks.

CASE 2.—I. N., a girl aged 15 years, was injured in a truck accident on June 11, 1947. Os calcis pin traction was instituted continuously over a period of two months. An open reduction

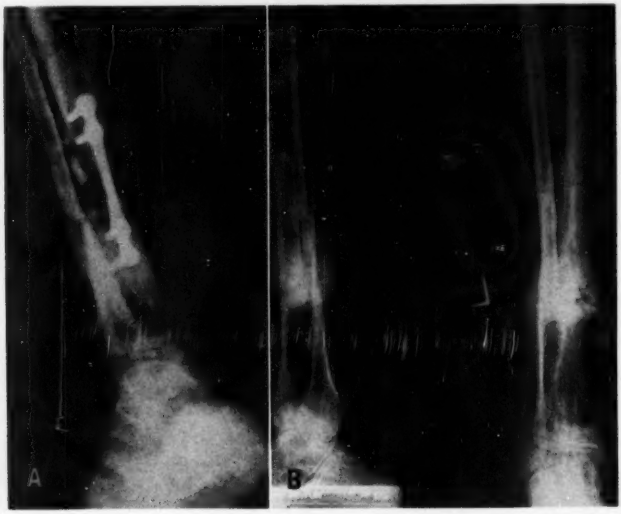

Fig. 4 (case 2).—*A*, preoperative appearance of nonunion of tibia. Marked separation of bone ends and osteoporosis are apparent. *B*, solid bony union present five months after operation.

was subsequently done, with the introduction of a plate and screws (fig. 4 *A*). The entire wound broke down, with active local drainage.

On her first admission to the Cook County Hospital, notable deformity of the foot existed, with ulceration of the heel and clawing of the toes. On November 20 we removed the plate and screws, the malposition of the foot and leg were corrected and a circular cast was applied from groin to toes. On March 5, 1948, frank nonunion was present, with roentgenologic evidence of severe osteoporosis of the tarsal and leg bones. On March 12 a simple onlay graft was placed lateral to the nonunion site and a cast was applied from the groin to the toes. Healing occurred in four months, and full weight bearing was started at the end of five months (fig. 4 *B*).

CASE 3.—J. C., a man aged 46, fell and fractured the lower third of his right tibia and fibula on Jan. 12, 1946. A cast was applied the same day and subsequently was replaced by skeletal pin traction. This was continued for eight weeks. A Parham-Martin band was then applied and removed after six weeks. When we first saw the patient there was frank nonunion of the tibia, and on May 9, 1947, a simple onlay graft was performed, the bone graft being taken from the proximal portion of the tibia. There was scarring, and local drainage through a pinpoint sinus

was present over the anterior tibial area. The postoperative course was uneventful, the cast being removed in 10 weeks. Weight bearing was begun in 12 weeks. Seven months after operation complete bony union of the tibia was present.

CASE 4.—C. C., a man aged 47, was struck by an automobile on Feb. 6, 1949, sustaining a fracture at the junction of the middle and lower third of the right tibia and at the upper third of the right fibula. Skeletal pin traction through the os calcis was instituted for eight weeks, and then a plaster cast was applied. Three months later a sequestrectomy was done for an exposed portion of the proximal tibia. Drainage persisted and an ulcer, 2 by 1 cm., was present over the lower third of the leg anteriorly. On September 9 a second sequestrectomy was done. On October 13 a simple bone graft was done (fig. 5) in the presence of a small draining sinus. A cast was applied from the groin to the toes. Healing was extremely slow, and weight bearing

Fig. 5 (case 4).—Roentgenographic evidence of bone healing at end of three and one-half months.

was not instituted until May 2, 1950. At the present time there is good clinical union and the patient is bearing weight without discomfort.

CASE 5.—B. S., a man aged 42, sustained a fracture of the left tibia and fibula on March 8, 1946. Three days after this injury an open reduction with single screw fixation was performed. Gross infection followed this procedure. Six weeks after the operation the screw was removed and a sequestrectomy was done. On his admission to the Cook County Hospital on Feb. 6, 1947, the operative wound was infected and draining profusely. Flail motion was present at the fracture site, and roentgenograms revealed a tibial separation of one inch (fig. 6*A*). The extremity was cold because of chronic local vasospasm. On March 14 a left lumbar sympathectomy was performed, with clinical improvement. The wound drainage, however, continued, and on April 1, 1947, a high fibular osteotomy was performed. The tibial bone ends were freshened and allowed to come in contact with each other. The wound continued to drain pro-

fusely. Amputation was seriously considered, but a further period of immobilization was carried out. In three months the sinus closed, but frank nonunion persisted (fig. 6 *B*). On August 8, 1948, a simple onlay graft was performed. In three months solid union was present (fig. 6 *C*), and weight bearing was begun two months later. At this time the patient has a solid union and no symptoms.

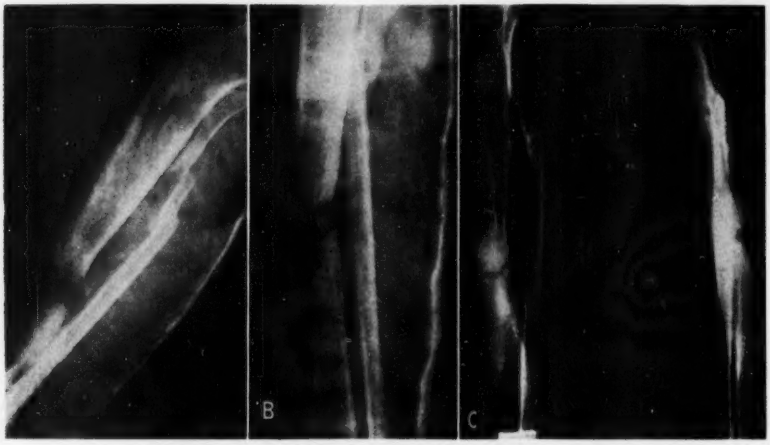

Fig. 6 (case 5).—*A*, frank nonunion of tibia, with 1 inch (2.5 cm.) separation of bone ends. *B*, after osteotomy of fibula, bone ends are seen in closer approximation. *C*, solid bony union of tibia three months after onlay bone graft.

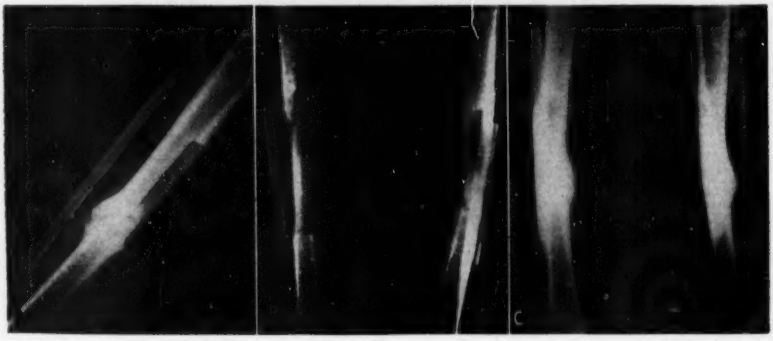

Fig. 7 (case 6).—*A*, nonunion of tibia at inferior end of donor graft area. *B*, onlay bone graft in place, adjacent to nonunion site. *C*, solid union of tibia seen after 10 weeks.

Case 6.—H. B., a man aged 39, sustained a fracture of the right tibia at the junction of the middle and lower thirds, in the region of a donor bone graft site (fig. 7 *A*). Nonunion ensued, and simple onlay bone graft was performed approximately six months later (fig. 7 *B*), the bone being taken from the opposite tibia. The right lower extremity was immobilized in a cast, and union took place in four months and two weeks. The nonunion healed uneventfully, and the patient is bearing weight without pain or discomfort at the present time (fig. 7 *C*).

Case 7.—T. K., a man aged 56, sustained a fracture of both bones of the right leg on June 23, 1946. Skeletal traction through the heel was applied for two weeks, and an open operative

reduction was attempted at this time, a single screw being used. A cast was applied, but nonunion and severe bowing resulted. In May 1947 a sliding bone graft, with screw fixation, was tried but failed, with gross infection. In October 1947 we first saw this patient, with frank nonunion and osteomyelitis of the tibia. A sequestrectomy was done, and the extremity was again encased in plaster. A simple onlay graft was done (his fourth operation!) in November 1947. After six months of immobilization, nonunion and frank drainage resulted. Amputation was then performed at the upper third of the leg.

SUMMARY AND CONCLUSIONS

Twenty-three patients with nonunion of the lower third of the tibia were treated with simple onlay bone graft. Bony union was obtained in 22 patients. One case required amputation for a persistent nonunion associated with osteomyelitis. Bone healing occurred in from eight to 21 weeks after operation. Of 13 cases in which ulcers or sinuses were present, healing took place in 10. Simple onlay bone grafts may be done in the presence of small, draining sinuses, local ulceration or even osteitis, if care is taken to avoid the adherent scar or the local sinus.

The procedure described is simple and short and results in good healing in the majority of cases of nonunion of the lower third of the tibia.

ABSTRACT OF DISCUSSION

DR. W. F. HOLCOMB, Oakland, Calif.: When I first received and read Dr. Miller's paper some weeks ago, I was much troubled as to what I might say in the way of discussion. My first impression was that, in reality, the method was not particularly new. Most of us, I believe, have carried out many methods of bone grafting, including fixation by wires, screws, sutures, bands, laying grafts in prepared slots and, finally, just allowing the graft to rest against the bone. Operations in the face of minor infections and sinuses have been carried out for at least 25 years, to my knowledge, so that this is not particularly new or unusual.

I then reviewed, in my mind, those operations of tibial grafting which I have carried out in the past few years. Without exception, no matter what the type of graft used, I have always done an osteotomy of the fibula and have also drilled the ends of the bone where there was eburnation or fibrous tissue formation. I then mentally reviewed the results which have been obtained, and certainly I cannot boast of anything like the results Dr. Miller has reported.

I must confess that no logical explanation comes to my mind of why a piece of medullary bone placed alongside a cortical surface will unite more rapidly and in a greater number of instances than if the surface was denuded or a slot prepared. The question presents itself of why it is poor surgical procedure to remove the scar between the ununited ends when so often that and nothing more has produced union. There is the problem, also, of why an osteotomy of the fibula should not be carried out when often that in itself will produce union without further operative procedure. Why should we not carry out all these procedures, as long as they are fairly simple, which, we have found in the past, tend to produce union where nonunion has existed?

Papers such as this, I believe, are of great value and show the fortitude of the man who is willing to stake his results on one procedure, thereby evaluating its efficacy. If Dr. Miller will give us some logical explanation of his magic, I will follow in his footsteps and attempt to emulate his results. If he does not, I am afraid I shall be a backslider, and the next time I have an ununited fracture at the junction of the middle and lower thirds of the leg I shall probably drill the ends and perform osteotomy of the fibula, as I have always done before.

DR. I. S. MCREYNOLDS, Houston, Texas: Dr. Miller has given an able presentation of a difficult problem. I believe that Dr. Phemister's original approach to this method of bone grafting was influenced chiefly by his desire not to have a firmly fixed graft attached to the tibia and also through his feeling that this type of approach was less traumatic and did not do so much to devitalize tissues as some of the other operative procedures.

The factor of a lack of surgical trauma in any nonunion of the tibia in this location, particularly in such cases as some of those which were shown by Dr. Miller, is of extreme importance.

I have had no personal experience with this type of operation but, having used iliac bone grafts in a somewhat similar manner in a rather large number of cases with gratifying results, I think the two methods have something in common.

The best place to put a graft on the tibia is, of course, on the lateral aspect, where there is a definite covering of muscles and soft tissues and where there is not the extreme postoperative tissue reactions following surgical exposure as there is in reflection of skin flaps from the anteromedial surface of the leg where the tibia is superficial. In cases in which there has been a previous operation, with scarring or poor circulation of the skin over the medial aspect of the tibia, there is much more likelihood of the skin in the line of the incision or in the area of previous scarring breaking down, and the incision should be lateral to the crest of the tibia.

DR. HAROLD E. CROWE, Los Angeles: Will you ask Dr. Miller to tell us how he corrected the bad position of that atrophic foot without changing the alinement of the fracture?

DR. DONALD S. MILLER, Chicago: It was simple to correct the deformity of the ankle joint. The angulation was not more than 10 degrees, and the toes came up without trouble. One favorable feature about these severe nonunions is that they have a good fibrous scar at the lower third of the tibia, and deformity does not generally occur. That has been our experience in Chicago.

This method is certainly not new. Dr. Phemister has used it many times, and we are just following his method. There is no magic about it. The operation is very simple, takes 15 or 25 minutes and generally results in a good nonunion.

CONGENITAL SHORT ESOPHAGUS

Review of Literature and Eight Original Cases, Including One Autopsy Report

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ALTHOUGH the short esophagus is no longer considered a rarity, its description in autopsy material is infrequent. In presenting the autopsy findings of a case in 1836, Bright,[1] although he did not use the term, described a case of thoracic stomach, with the esophagogastric junction situated at the level of the fourth thoracic vertebra. Kelly [2] summarized nine clinical cases in 1931 under the heading "congenital shortening of the esophagus." Since Morison [3] added a case found at autopsy in 1930 four additional cases have been presented by Jacob, Tweedie and Negus,[4] French [5] and Rennie, Land and Scott Park.[6] During this period clinical reviews appeared by Clerf and Manges,[7] Monkhouse and Montgomery,[8] Dunhill,[9] Chamberlin,[10] Harrington,[11] Polley,[12] Johnstone,[13] Dick and Hurst,[14] Smithers,[15] Allison,[16] Feldman [17] and Rennie and others.[6]

From the Department of Surgery, Alexander Blain Hospital, Detroit.

1. Bright, R.: Account of a Remarkable Misplacement of the Stomach, Guy's Hosp. Rep. **1**:598, 1836.

2. Kelly, A. B.: Congenital Stenosis of Esophagus with Diaphragmatic Hernia of the Stomach, Acta oto-laryng. **15**:368, 1931. Findlay, L., and Kelly, A. B.: Congenital Shortening of Esophagus and Thoracic Stomach Resulting Therefrom, J. Laryng. & Otol. **46**:797, 1931.

3. Morison, J. M. W.: Diaphragmatic Hernia, Proc. Roy. Soc. Med. **23**:1615, 1930.

4. Jacob, F. H.; Tweedie, A., and Negus, V. E.: Congenital Shortening of Esophagus, J. Laryng. & Otol. **48**:486, 1933.

5. French: Postscript to publication of Dick and Hurst.

6. Rennie, J. B.; Land, F. T., and Scott Park, S. D.: The Short Esophagus: A Review of 31 Cases, Brit. M. J. 1949, p. 1443.

7. Clerf, L. H., and Manges, W. F.: Congenital Anomalies of Esophagus, with Special Reference to Congenitally Short Esophagus with Portion of Stomach Above Diaphragm, Ann. Otol., Rhin. & Laryng. **42**:1058, 1933; Congenitally Short Esophagus, J. A. M. A. **102**:2008 (June 16) 1934.

8. Monkhouse, J. P., and Montgomery, S. K.: Report of 7 Cases of Partial Thoracic Stomach with Short Esophagus, J. Laryng. & Otol. **48**:743, 1933.

9. Dunhill, T.: Diaphragmatic Hernia (Arris and Gale Lecture), Brit. J. Surg. **22**:475, 1935.

10. Chamberlin, D. T.: Peptic Ulcer of the Esophagus, Am. J. Digest. Dis. **5**:725, 1938.

11. Harrington, S. W.: Diagnosis and Treatment of Various Types of Diaphragmatic Hernia, Am. J. Surg. **50**:381, 1940.

12. Polley, H. F.: Congenital Short Esophagus with Thoracic Stomach and Esophageal Hiatus Hernia, J. A. M. A. **116**:821 (March 1) 1941.

13. Johnstone, A. S.: Some Radiological Observations on Post-Cricoid Obstruction and Anemia, Brit. J. Radiol. **14**:177, 1941.

14. Dick, R. C. S., and Hurst, A.: Chronic Peptic Ulcer of the Esophagus and Its Association with Congenitally Short Esophagus and Diaphragmatic Hernia, Quart. J. Med. **11**:105, 1942.

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(Footnotes continued on next page)

Shortness of the esophagus has long been considered a congenital lesion, but recently evidence for an acquired etiology has been presented (Johnstone,[13] Smithers,[15] and Rennie and others [6]). Congenital short esophagus requires sharp distinction from hiatus hernia, since with the former the stomach has never occupied its normal position in the abdomen. Theoretical explanations for congenital shortness of the esophagus have been proposed by many authors. Bund,[18] Bailey,[19] Akerlund,[20] and Jackson and Jackson [21] considered it secondary to failure of fixation of the lower end of the esophagus resulting from delayed closure of the right or left pleuroperitoneal recess. Tonndorf [22] and Keith [23] considered esophageal hypoplasia and arrested descent of the stomach the primary defect. The theory of an acquired origin postulates the presence of a large esophageal hiatus, either congenital or acquired, which permits a sliding herniation of the stomach into the mediastinum. This displacement interferes with the cardiac valvular mechanism, which is a function of normal position, so that reflux of acid-peptic secretions from the stomach into the esophagus becomes possible despite a normal cardiac sphincter (Dick and Hurst [14]). The inflammation and cicatrization produced by this reflux of gastric secretions are considered capable of producing the shortened esophagus. The congenital short esophagus, as a result of the same mechanism of reflux, is also subject to the complications of acid-peptic digestion. Other complications associated with displacement of the stomach have been outlined by Dunhill.[9] Since all factors tend to increase the herniation of the stomach and since the lesser curvature of this organ is relatively fixed, rotation about its own axis results. Dunhill stated that rotation about the long axis of the stomach might occur and result in obstruction of the middle third, with the production of two gastric loculi. This situation or angulation at the diaphragmatic opening he considered would produce overdistention of the cardiac loculus or the proximal gastric pouch. The latter development occurred in one of the cases to be presented.

REVIEW OF MATERIAL

During the period 1943 to 1949, eight cases of "congenital short esophagus" have been studied.

CASE 1 (fig. 1).—J. C., a man aged 56 years, had complained of midline pain in the chest, epigastric distress and intermittent dysphagia for 30 years. A diagnosis was established by roentgen examination in 1943. The patient was lost to the follow-up clinic, but investigation revealed that he had died in another hospital on Jan. 6, 1945. Dyspnea, weakness and an inability to swallow characterized the week prior to his death. No autopsy was performed. Death was

16. Allison, P. R.: Peptic Ulcer of the Esophagus, Thorax **3**:20, 1948.

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18. Bund, R.: Ein Fall von rechtsseitiger Hernia diaphragmatica mit Austritt des Magens in den persistierenden Rezessus pneumatoentericus dexter, Frankfurt. Ztschr. f. Path. **21**:243, 1918.

19. Bailey, P.: A Case of Thoracic Stomach, Anat. Rec. **17**:107, 1919.

20. Akerlund, A.: Die anatomische Grundlage des Röntgenbildes der sogen. "erworbenen Hiatusbrüche," Acta radiol. **14**:523, 1933.

21. Jackson, C., and Jackson, C. L.: Peroral Gastroscopy Including Examination of the Supradiaphragmatic Stomach, J. A. M. A. **104**:269 (Jan. 26) 1935.

22. Tonndorf, W.: Wahre Zwerchfellhernien als Folge einer Wachstumshemmung der Speiserohre, Deutsche Ztschr. f. Chir. **179**:259, 1923.

23. Keith, A.: Dunhill.[9]

attributed to coronary occlusion, but no objective evidence was presented for this diagnosis. It has long been known that gastrocardiac symptoms associated with a short esophagus can simulate coronary disease (Von Bergmann,[24] Polley [12]).

CASE 2 (fig. 2).—E. F., a man aged 58 years, had experienced midline pain in the chest, epigastric distress and dysphagia with occasional emesis intermittently for 10 years. Hematemesis and melena were noted. The diagnosis was established in 1946 by roentgen examination. A definite correlation of symptoms to emotional stress was noted. He was placed on a peptic ulcer regimen, with little benefit. Development of achlorhydria was associated with a diminution of symptoms in 1946. There have been no complications to the present time.

CASE 3.—B. G., a woman aged 65 years, had noted intermittent dysphagia, nausea and epigastric distress during a 12 month period. The diagnosis was established by roentgen examination in 1946. Frequent small feedings had been resorted to by the patient and had resulted in partial relief of symptoms, but moderate weight loss and weakness had developed. A medical regimen controlled the patient's symptoms until her death in January 1948, at another hospital. No autopsy was performed.

Fig. 1 (case 1).—Roentgenogram illustrating the shortened esophagus and its entry into the proximal portion of the stomach situated in the posterior mediastinum. Note the constriction at the esophagogastric junction.

CASE 4.—M. J., a woman aged 58 years, had been troubled by chest pain, epigastric distress and nausea and vomiting in association with eating for the previous 28 years. The diagnosis was established by roentgen examination and esophagoscopy in 1948. Antispasmodics and antacids were given and benefited the patient but failed to give complete relief. Many emotional problems had been present, and a good correlation of symptoms with emotional stress had been noted. Hematemesis had occurred recently. The patient's condition was reasonably well controlled by medical management. She had remained free of complications to the present time.

CASE 5.—M. W., a woman aged 48 years, had suffered with epigastric distress, sensitive stomach and nausea and vomiting in relation to eating for as long as she could remember. The diagnosis was established by roentgen examination in 1948. She was subject to long remissions and had noted that emotional stress was related to her exacerbations. Her recent difficulty was related to anxiety associated with the development of tic douloureux in her mother. She has been satisfactorily managed to date by a medical regimen.

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24. Von Bergmann, G.: Das "epiphrenale Syndrom," seine Beziehung zur Angina pectoris und zum Kardiospasmus, Deutsche med. Wchnschr. **58**:605, 1932.

Case 6 (fig. 3).—W. M., a woman aged 67 years, had noted epigastric pain and distress, dysphagia and vomiting intermittently for three years. Symptoms were present only when she was emotionally upset. The diagnosis was established in 1948 by roentgen examination. Excellent

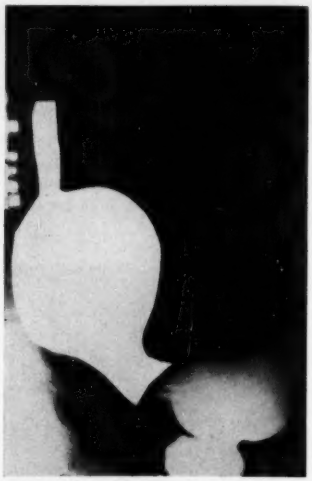

Fig. 2 (case 2).—Roentgenogram showing the esophagus entering directly into a large globular, proximal gastric pouch in the posterior mediastinum. The portion above the diaphragm has been artificially emphasized.

Fig. 3 (case 6).—Roentgenogram illustrating a straight esophagogastric junction and displacement of the proximal portion of the stomach above the diaphragm.

control has been obtained by the use of antispasmodics, antacids and allied medical measures up to the present time.

Case 7.—J. C., a man aged 55 years, has had a "sensitive stomach" all his life. Periodic difficulty with epigastric distress, dysphagia and midline retrosternal pain in the chest had been present all his life. It was necessary for him to follow a curtailed diet and devote special

Fig. 4 (case 8).—Roentgenogram illustrating a short esophagus with constriction at the esophagogastric junction. Compare with figures 5 and 6 of the same case.

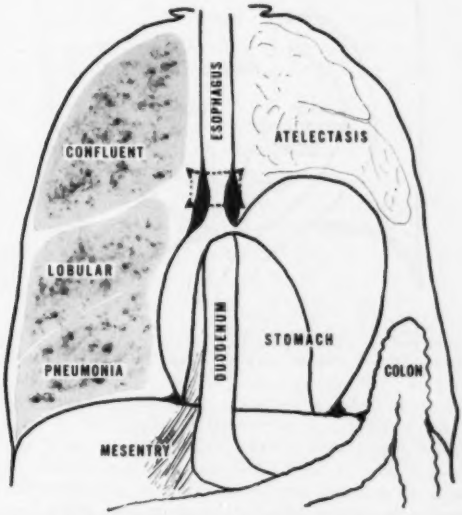

Fig. 5 (case 8).—Sketch of the thoracic findings at the time of the necropsy. Note the following features: the dotted outline of the seventh thoracic vertebra indicating the junctional level of the esophagus and the stomach; fixation points at the esophageal hiatus that contributed to the 180 degree angulation of the midportion of the stomach, with the production of a proximal and distal gastric pouch; the distended proximal gastric pouch that contained 1,500 cc. of fluid. The persistent duodenal mesentery allowed migration of the pyloric portion of the stomach almost to the level of the seventh thoracic vertebra. The darkened area at the esophagogastric junction denotes the dense fibrous reaction at this level.

attention to swallowing. His symptoms were markedly aggravated by emotional tension. The diagnosis was established in 1949 by roentgen examination. He was improved by the introduction of antispasmodics and antacids into his self-imposed regimen. There have been no complications to the present time.

CASE 8 (fig. 4).—H. B., a 55 year old white man, was first seen in February 1948 because of dysphagia which had been present intermittently for more than 10 years. Esophageal obstruction resulting in emesis with soft solids such as mashed potatoes preceded his admission. Esophagoscopy and roentgen examination revealed a constricted esophagogastric junction at the level of the seventh thoracic vertebra. Because the lumen at this junction was narrowed to 5 mm., a cardioplasty was performed. The symptoms of esophageal obstruction were relieved, and the patient was discharged on an ulcer regimen.

Retrosternal pain developed, and weakness, tarry stools and hematemesis caused his readmission one month later. The hemoglobin content was found to be 4.8 Gm. per 100 cc. of blood.

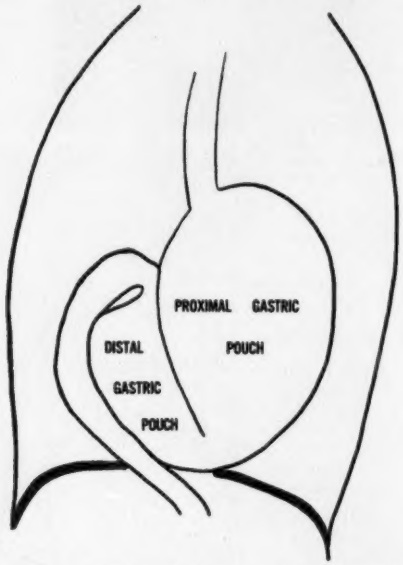

Fig. 6 (case 8).—Sketch of a left lateral view of the stomach. Total thoracic displacement, folding of the midportion and formation of a proximal and distal gastric pouch are indicated.

Massive hematemesis, in amounts up to 1,000 cc., continued for seven days, and roentgen ray examination revealed regurgitation of barium sulfate at the site of the cardioplasty. Blood replacement and medical management produced sufficient improvement to allow his discharge.

He was readmitted because of acute hematemesis five months later. During the interval intermittent dysphagia had occurred, and he had had two episodes of hematemesis associated with transient obstruction by a bolus of food. An esophagogram at this time suggested an ulcer at the esophagogastric junction. Barium enema revealed herniation of the splenic flexure of the colon through the diaphragm. A sippy regimen produced a prompt improvement, which led to the patient's discharge on Sept. 14, 1948.

He did not return until May 10, 1949, when repeated violent emesis, present three days and as frequent as 25 times daily, occasioned his readmission. He had ignored dietary precautions and had been relying on antacids to control epigastric and retrosternal burning pain. Intermittent dyspnea developed for the first time during this interval, and it is noteworthy that gastrointestinal bleeding was not a feature of this episode. Dyspnea and cyanosis became progressively worse, and he died from asphyxia on May 21, 1949.

The important gross pathologic features were in the thorax (fig. 5). The esophagus joined the cardia of the stomach at the level of the seventh thoracic vertebra, where there was marked fibrotic thickening of the wall and narrowing of the lumen without obstruction. The distance between the alveolar margins and the esophagogastric junction was 25 cm. Ulceration of the esophagus extended proximally to 4 cm. The stomach was entirely within the thorax because of folding which superimposed the pylorus on the esophagogastric junction (fig. 6). This striking deformity was possible because of the unusual mobility imparted to the pyloric portion by a persistent duodenal mesentery. The midportion of the stomach was fixed by a cicatrix to the lateral margins of the widened esophageal hiatus and supplied a fixed point about which folding had taken place. Acute angulation at this level of fixation had produced a cardiac and pyloric gastric loculus or pouch. The cardiac portion was markedly distended, contained 1,500 cc. of fluid and occupied much of the left thoracic cavity. Gastritis, most pronounced at the esophagogastric junction, was noted. A left lateral diaphragmatic defect permitting herniation of the splenic flexure and two loops of small intestine was present. The left lung weighed 100 Gm. as a result of a compression atelectasis produced by the displacement of abdominal organs. The right lung weighed 900 Gm. and showed a confluent lobular pneumonia. Histologic examination confirmed the gross pathologic diagnoses. Infarction of a portion of the gastric wall was the only additional finding of interest.

The final diagnosis in this case was congenital short esophagus complicated by loculation, obstruction and infarction of the stomach, displacement of the stomach and portions of the colon and the small intestine into the left thoracic cavity, ulcerative esophagitis, atelectasis of the left lung and confluent lobular pneumonia of the right lung.

COMMENT

Shortness of the esophagus is demonstrable by roentgenologic examination and/or esophagoscopy. The change in mucosal pattern that characterizes the esophagogastric junction is confirmed by biopsy specimens, and thus an accurate placement of the junction is possible by direct measurement. That shortening may by transient and capable of resolution is apparent from a recent report by Rennie and others.[6] They reported two cases observed at autopsy, and in neither case was a short esophagus demonstrated despite conclusive antemortem evidence of its presence. Smithers [15] considered that the paucity of autopsy descriptions, despite frequent clinical diagnoses, indicated that transient, acquired shortening rather than the permanent congenital type was the common situation. In the present series there were three deaths, and the single autopsy revealed a short esophagus. The esophagogastric junction had not changed from that shown clinically and was at the level of the seventh thoracic vertebra. This has been previously observed to be a remarkably constant junctional point in congenital cases (Brown Kelly,[2] Marks [25]). Scarring and ulceration were considerable at the time of death but were not striking at the time of operation, and symptoms suggesting esophageal digestion by acid-peptic secretion developed subsequent to surgical intervention. It was inferred, therefore, that shortening preceded the development of pronounced scarring and was of the congenital type. The demonstration of a persistent duodenal mesentery favored this view.

Dysphagia, pain and vomiting in relation to eating were characteristic symptoms found in this series. Initiation and aggravation of symptoms by emotional tension have not been stressed in previous reviews. The relation of emotion to symptoms, periodicity of symptoms and the possibility of transient shortening becomes more logical when assessed in the light of recent reports,[26] which demon-

25. Marks, J. H.: Diaphragmatic Hernia and Associated Conditions, Am. J. Roentgenol. **37**:613, 1937.

(Footnotes continued on next page)

strated contraction of the longitudinal muscle layer of the esophagus, with consequent shortening of this organ, in response to both direct and reflex stimulation of the vagus nerve in animals. Herniation of the stomach through the esophageal hiatus was also produced. Symptomatic improvement with the use of antispasmodics and allied medical measures has therefore been placed on a more rational basis.

Since there is a tendency toward increased herniation, with its attendant risk of torsion, loculation, obstruction or even strangulation, a situation may develop which is no longer controlled by conservative management. The complications of reflux of acid-peptic secretions may also indicate the need for surgical intervention. While long considered a lesion not amenable to surgical treatment, the shortened esophagus has been successfully dealt with by several methods. Plastic procedures,[27] elevation of the diaphragm,[11] replacement of the stomach [28] and gastrectomy [29] have been employed.

Prevention of acid-peptic reflux and elimination of mechanical complications of the displaced stomach are the primary objectives in therapy. If these objectives can be obtained by replacement of the stomach and restoration of the cardiac valvular mechanism, this is the procedure of choice. When this is not possible, the procedure fulfilling these aims with least risk, namely, subtotal gastric resection, appears most logical. If stenosis of the terminal portion of the esophagus has preceded elimination of acid-peptic irritation, it may respond to dilatation, as in the case described by Wangensteen.[29a] The inadequacy of lesser procedures is apparent from the postoperative course of the patient in this series treated by plastic revision of the esophagogastric junction. The obstruction was relieved, but the reflux of gastric content was aggravated. The hazards associated with the mechanical complications of gastric displacement were not dealt with, and a fulcrum for acute angulation was introduced. The terminal episode in this case was precipitated by acute dilatation of the proximal gastric pouch and resulted in atelectasis of the left lung. When pneumonia developed in the right lung the patient died of asphyxia.

SUMMARY

Eight cases of "congenital short esophagus" have been briefly described. The history and autopsy findings of one case have been presented in detail. The role of emotional stress and a possible mechanism for its influence have been discussed in relation to exacerbations and remissions of symptoms. Uncomplicated cases were best managed by a medical regimen. For the complicated case requiring surgical intervention, replacement of the stomach into the abdomen was considered ideal and subtotal gastric resection the treatment of choice when fixation or shortening prevented such replacement.

26. Rall, J. E.; Gilbert, N. C., and Trump, R.: Effects of Vagus Stimulation on Longitudinal Fibers of Stomach and Esophagus, Quart. Bull., Northwestern Univ. M. School **19**:194, 1945. Dey, F. L.; Gilbert, N. C.; Roskelley, R. C., and Trump, R.: Effect of Stimuli Originating in Upper Abdomen in Causation of Reflex Shortening of Esophagus, Proc. Central Soc. Clin. Research **18**:8, 1945. Dey, F. L.; Gilbert, N. C.; Trump, R., and Roskelley, R. C.: Reflex Shortening of Esophagus in Experimental Animal with Production of Esophageal Hiatus Hernia, J. Lab. & Clin. Med. **31**:499, 1946.

27. Gordon Taylor, G., in discussion of Morison, J. M. W.: Diaphragmatic Hernia, Proc. Roy. Soc. Med. **23**:1615, 1930.

28. Harrington.[11] Allison.[16]

29. (*a*) Wangensteen, O. H., and Leven, N. L.: Gastric Resection for Esophagitis and Stricture of Acid-Peptic Origin, Surg., Gynec. & Obst. **88**:560, 1949. (*b*) Allison.[16]

EXPERIENCES WITH ANURIA AND OLIGURIA

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THE TREATMENT of anuria and oliguria has received increasing attention in the past few years, probably as a result of the introduction of the sulfonamides and because of the occurrence of shock and blood transfusion reactions in the past war. The mortality associated with acute suppression of the urine has been high in the past, ranging from 20 to 50 per cent. A good part of this mortality has been due to poor management, probably resulting in a large measure from misunderstanding concerning the basic physiological principles involved.

Acute suppression of the urine may be the result of (1) mechanical blockage, (2) dehydration, (3) action of poisons on the kidneys, (4) lower nephron nephrosis or (5) hepatorenal syndrome. Mechanical blockage to the outflow of urine is most commonly caused by stones or sulfonamide crystals and has received emphasis for some time from the urologists. The lower nephron nephrosis type of urinary suppression has been more recently described. Burnett, Snyder and others, on the basis of material obtained at autopsy in known cases of renal failure following injury or transfusion reaction, have pointed out that the significant pathological changes in the renal parenchyma, while not necessarily specific, are frequently located in the distal tubular segments of the nephron units.

The mechanism of renal failure in the so-called hepatorenal syndrome is still obscure. Acute suppression of the urine has been reported 343 times, with 143 deaths, in the available English literature (January 1940 to January 1950). The number of each type of case is as follows:

1. Mechanical blockage	145
2. Lower nephron nephrosis or actions of poisons on the kidneys	193
3. Hepatorenal syndrome	5

Anuria caused by sulfonamides has been reported treated by several of the methods listed in table 1. From this table it would appear that as a general rule conservative measures result in a lower mortality. However, in some of these cases relief of the mechanical blockage by nephrostomy or catheterization is required.

Oliguria and anuria as a result of various poisons or of anoxia induced by shock have been reported a total of 156 times, with 65 deaths.

It appears that the more conservative measures with low fluid intake result in lower mortality. The forcing of fluids has resulted in such a high mortality rate that this treatment is being discontinued. Renal block by calculi was reported 29 times, with two deaths, in this series. The patients require relief of the mechanical obstruction. The hepatorenal syndrome has been reported five times, with a fatality in each instance.

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The following are case reports from local Houston hospitals:

CASE 1.—L. B., a 29 year old white man, was admitted to the hospital because of a ruptured appendix, which was removed in the first 24 hours following admission. The first three postoperative days he seemed to do well. He received during this time 2,000 cc. of dextrose and distilled water and 1,000 cc. of saline solution plus an unmeasured amount of fluids orally. The urine output was not measured. On the third day he became distended, oral intake was discontinued and intravenous administration of fluids, 3,000 cc. of dextrose and distilled water and 1,000 cc. of saline solution for each 24 hours, was started. Urine output was 2,500 cc. during the next eight days. At the end of the eighth postoperative day he had a sudden elevation of temperature and was in a shocklike state for a few hours. After this he apparently revived to some extent, but the urine output diminished to 558 cc. during the next four days. During this four day period he received 20 liters of fluid. He died on the thirteenth postoperative day of pulmonary edema. The autopsy findings were bilateral hydrothorax, bilateral massive pulmonary

TABLE 1.—*Methods of Treatment of Sulfonamide Anuria*

Treatment	Number of Cases	Deaths
Forcing of fluids intravenously	4	4
Intestinal lavage	6	6
Nephrostomy	5	0
Diathermy *	7	0
Spinal anesthesia *	4	0
Catheterization of the ureters	31	1
Renal decapsulation *	10	1
Renal pedicle block *	126	1
Conservative treatment *	23	3

* 1,000 to 1,500 cc. of fluid a day.

TABLE 2.—*Treatment of Oliguria and Anuria Due to Poisons*

Treatment	Number of Cases	Deaths
Conservative treatment *	20	1
Renal pedicle block *	30	5
Forcing fluids intravenously (more than 3,000 cc. a day)	47	38
Renal decapsulation	36	12
Intestinal lavage	23	9

* 1,000 to 1,500 cc. of fluid a day.

edema and congestion of all organs. Although this patient was seriously ill, he might have had more chances of survival if the administration of fluid had not been so vigorous.

CASE 2.—J. N., a 42 year old white woman, was admitted to the hospital because of nausea, vomiting and jaundice. During the first 14 hospital days the urine output was 495 cc. During this time she received 500 to 1,000 cc. of fluids intravenously per day. On the fourteenth hospital day catheters were placed into each side of the peritoneal cavity and irrigated with Tyrode's solution at the rate of 100 cc. an hour. During the next four days the chlorides, carbon dioxide, total base and nonprotein nitrogen levels returned to within normal limits and 762 cc. of urine was excreted. She continued to receive from 500 to 1,000 cc. of fluids intravenously a day, most of which was lactate Ringer's solution. She died on the nineteenth day after her admission. An electrocardiogram on the last day of her survival was suggestive of a low serum potassium content. However, this interpretation was not made until several months after her death. This patient had a type of syndrome that has sometimes been classed as the hepatorenal syndrome of anuria associated with jaundice and liver failure. Judging from the tests done, the chemical composition of the blood returned to normal during the peritoneal lavage. The electrocardiographic changes suggested that death could have been due to hypopotassemia.

CASE 3.—B. J. G., a 30 year old Mexican, was admitted to the hospital to undergo an extrapleural pneumothorax for tuberculosis. Before operation the hematocrit value was 31, and he went into severe shock during the operative procedure. After operation the urine output ranged from 60 to 300 cc. a day, with a total of 1,500 cc. during the next 10 days. During this time the patient received 1,000 to 1,500 cc. a day of dextrose in distilled water as replacement therapy. The electrolyte pattern was ascertained daily and corrected as necessary. On the eleventh day the patient began to pass a large amount of urine, which steadily increased from 2,800 cc. on the eleventh day to 7,700 cc. by the seventeenth postoperative day. During this time he was given lactate Ringer's solution in volume equal to the daily output of urine. On the seventeenth postoperative day the serum potassium level was 2.8 milliequivalents. As the patient was taking fluid by mouth it was felt that the potassium deficit could be corrected in this way, and three days later the potassium level was 3.8 milliequivalents. He went on to complete recovery. The electrolyte changes were followed more carefully in this case than in some of the others because of the availability of better laboratory facilities. Potassium intake should be increased during the period of increased urine excretion because of excessive loss at this time. The facilities of a laboratory to follow the electrolyte pattern more closely are advantageous, and the treatment given in this case will in general be used for anuria and oliguria in the future. We felt that the shock which occurred during the operation might have been prevented or lessened by better preoperative preparation with blood transfusion. On the basis of experiences of my colleagues and me with tuberculosis, the patient should have received 2,500 cc. of blood before surgical intervention (Hay, Hay and Jenkins).

CASE 4.—A. S., a 47 year old white man, sustained fractures of both legs in an automobile accident. His urine output during the first three days after admission to the hospital was 200 cc. There was no more urine output, and he was given from 3,000 to 5,000 cc. of fluids intravenously daily. He died on the seventh hospital day with signs of pulmonary edema and cardiac failure, apparently drowned by too much fluid. Autopsy was not done.

CASE 5.—W. J., a 61 year old white woman, underwent a cholecystectomy for gallstones and a nephrectomy for stag-horn calculus. After the operation the urine output varied from 15 to 200 cc. daily, with a total of 850 cc. during the first five postoperative days. On the sixth day she passed 450 cc. of urine, and after this her recovery was rapid. She received from 1,000 to 1,500 cc. of dextrose in distilled water each day during the period of anuria and enough fluids to supplement the urinary output during the period of diuresis.

CASES 6 to 18.—Thirteen patients whose ages were 8, 40, 70, 2, 4, 63, 38, 58, 68, 31, 24, 4 and 11 had sulfonamide anuria of from two to five days' duration. Four underwent cystoscopy and three nephrostomy. All were treated with a low fluid intake of from 1,000 to 1,500 cc. each day, and all recovered. Many of these patients require urethral catheterization to relieve the sulfonamide crystal blocks, and in some nephrostomy is required because of inability to pass urethral catheters. It has been demonstrated that some patients sustain oliguria or anuria from sulfonamide without mechanical blockage; however, as urethral catheterization is an innocuous procedure it would seem to be worth while in all cases of anuria caused by sulfonamides.

COMMENT

From this review of the literature and from our own experience it seems that the mortality from acute suppression of urine is sometimes high, especially if large quantities of fluids are given intravenously. Most of the patients with blockage, from either stones or sulfonamides, are promptly relieved by catheterization or nephrostomy. In many of these the urinary suppression is of short duration, and the maintenance of fluid and electrolyte balance is frequently not a great problem. The tubular damage associated with the lower nephron nephrosis type of syndrome is reversible, and recovery with adequate function may ensue in from seven to 14 days. The maintenance of fluid and electrolyte balance during these prolonged periods of anuria and diuresis is difficult without laboratory facilities. However,

the electrocardiogram will sometimes reflect the potassium changes enough for treatment, and if overhydration is avoided and acidosis corrected, the mortality during the period of urinary suppression can be lowered, even in the absence of an elaborate laboratory. The administration of potassium and fluids equal to urinary output during the period of diuresis may further lower mortality.

Besides the precipitating causes of urinary suppression, such as mechanical block and lower nephron nephrosis, there are predisposing causes, such as dehydration, cirrhosis, low blood volume (Hay, 1948) and high salt intake (Collier and others, 1944). In the future we hope to prevent as many cases of urinary suppression as we can by seeing that our patients have correction of blood volume deficits, adequate hydration and a low salt intake in the immediate postoperative period.

Procedures such as renal pedicle blocks, spinal anesthesia, sympathectomy, renal decapsulation, intestinal lavage and the use of artificial kidneys need further study before they can be evaluated. Drugs such as alcohol, mercurial diuretics, aminophylline and sodium sulfate have not proved to be of definite benefit in stimulating renal function.

SUMMARY

Eighteen cases of acute urinary suppression are reported in which there were three deaths. Two of these deaths were due to the administration of too much fluid. The other death occurred in a patient with jaundice and liver failure. In this patient low serum potassium was a contributory cause of death.

Thirteen of the 15 survivors had sulfonamide anuria. Most of these required relief of the obstruction by urethral catheterization or nephrostomy. The other two survivors received a low fluid intake during the period of urinary suppression and enough fluids to prevent dehydration during the period of diuresis.

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NEUROFIBROMA OF THE STOMACH AND ASSOCIATED GASTRIC ULCER

Report of a Case

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NEUROFIBROMA of the stomach is a relatively rare benign tumor. This fact alone seems to warrant a presentation of this subject, with a report of a case in which there was also an associated benign gastric ulcer below the stalk of the tumor.

The tumor was described for the first time by Askanazy.[1] A survey of the literature revealed an incidence of neurofibroma of less than 5 per cent among all benign tumors of the stomach reported. Minnes and Geschickter[2] in 1936 collected 931 reported cases of benign tumors, of which 102 were classified as neurofibromas. Paul and Chapman,[3] in 1,500 consecutive gastroscopic examinations, found only one neurofibroma, whereas Judd and Hoerner[4] found a neurofibroma in 50 cases of benign gastric tumors. At the Lahey Clinic during a five year period ending 1943[5] only one case of neurofibroma was found among 464 patients operated on for gastric neoplasm. Root[6] reported in 1942 that among 250,000 admission records only three cases of neurofibromas of the stomach were found. West and Knox[7] in 1948 reported six cases of neurofibroma. Tate and Fusaro[8] and Ellis and others[9] recently reported one case each.

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Jentzer, A., and Fatzer, H.: Case of Ganglioneurofibromatosis of Mesentery and Intestines with Malignant Degeneration, Schweiz. med. Wchnschr. **67**:569, 1937.

2. Minnes, J. F., and Geschickter, C. F.: Benign Tumors of the Stomach, Am. J. Cancer **28**:136, 1936.

3. Paul, W. D., and Chapman, D. W.: Neurofibroma: A Gastroscopic Report, Am. J. Digest. Dis. **12**:258, 1945.

4. Judd, E. S., and Hoerner, M. T.: Benign Tumors of the Stomach, Am. J. Surg. **31**:427, 1936.

5. Marshall, S. F., and Aronoff, B. L.: Symposium on Gastro-Intestinal Surgery: Tumors of the Stomach, S. Clin. North America **24**:607, 1944.

6. Root, J. C.: Benign Gastric Tumor: Case Report of Neurofibroma, Cleveland Clin. Quart. **9**:45, 1942.

7. West, J. P., and Knox, G.: Neurogenic Tumors of the Stomach, Surgery **23**:450, 1948.

8. Tate, R. W., and Fusaro, W. J.: Neurofibroma of the Stomach, Am. J. Surg. **75**:607, 1948.

9. Ellis, J. T.; Windham, S. W., and Latiolais, S. G.: Neurofibroma of the Stomach: A Case Report, Surgery **25**:752, 1949.

The most significant factors to be emphasized from the clinical standpoint are, first, the tendency of the gastric mucosa over the tumor to ulcerate and cause serious bleeding and, second, the possibility that the tumor may become malignant. In several instances the growth may reach a good size, and the majority of them ulcerate. However, in the case presented here the ulcer was below and adjacent to the tumor stalk. This combination of lesions was not previously described in the literature.

Pyloric obstruction may result in many cases because the tumor frequently originates in the prepyloric region and grows to a large size, thereby obstructing the outlet of the stomach. Over 50 per cent of the patients have complaints referable to the stomach, such as indigestion, nausea, vomiting and belching. In approximately 25 per cent of the cases the presenting complaint is hematemesis and/or tarry stools.

These lesions can be demonstrated and found by the roentgenologist and the gastroscopist. However, in many cases, as in the one being reported, the lesion may be so small that in order to find it by oral barium studies the roentgenologic technic must be meticulous. The barium sulfate should be introduced in small amounts so as to outline the stomach and not fill it to capacity. A filling defect produced by the intramural tumor, with rugal patterns overlying the defect, is found. This characteristic is due to the fact that the tumor grows outward toward the lumen of the stomach and thereby displaces the mucosa over it. In many of the cases reported a central niche was seen on roentgenographic examination. The ulcer is usually not deep, has a narrow mouth and is branching in the deep portion. There is usually an absence of spasm, which is so frequently seen in cases of gastric carcinoma and ulcer. In these cases the peristalsis passes over the filling defect.[9]

In the final analysis, a positive diagnosis of neurofibroma of the stomach is dependent on the microscopic examination. Even at the time of exploration, the operator cannot make an absolute diagnosis. He usually can state that the lesion is benign. The microscopic appearance of this lesion is the same as that of neurofibromas found elsewhere in the body. Most pathologists agree that the lesion develops in the wall of the stomach and displaces the gastric mucosa upward. The exact layer of origin is debatable. Some authorities are of the opinion that it arises from the gastric plexuses found between the muscle layers. Askanazy[1] stated that the nerve elements within the tumor are of sympathetic origin. It is generally agreed by the pathologists that the tumors do not arise from the axis cylinder. There is a disagreement as to whether they arise from the sheath of Schwann or from the supporting connective tissue.

The tumors may undergo malignant changes, forming a neurogenic sarcoma. Lahey and Colcock,[10] Paul and Chapman[3] and Walters[11] indicated that such changes may occur. In view of this possibility, the fact that the lesion may produce

10. Lahey, F. H., and Colcock, B. P.: Diagnosis and Surgical Management of Leiomyomata and Leiomyosarcomata of the Stomach, Ann. Surg. **112**:671, 1940.

11. Walters, W.: Benign and Malignant Tumors of the Stomach, Rocky Mountain M. J. **36**:770, 1939.

pyloric obstruction and the fact that in a great number of cases hemorrhage occurs, the treatment advocated is surgical excision. A local wide excision or sleeve resection of the stomach can be accomplished if the lesion does not appear malignant. If there is any doubt, gastric resection should be performed.

REPORT OF A CASE

O. C. R., a white man, 59 years of age, was admitted to the surgical service on May 22, 1950, for the treatment of a hernia in the right inguinal area. During the routine examination, it was found he had lost 10 pounds (4.5 Kg.) in weight during the past six months. He had mild indefinite gastrointestinal complaints. He also stated he had noticed blood in his stools on occasions during this period.

Fig. 1.—Roentgenogram of stomach after barium enema showing tumor at point of arrow.

The physical examination revealed only the presence of a right indirect inguinal hernia. The laboratory studies revealed a normal blood count. Stools were negative for blood, and gastric analysis revealed 15 degrees of free hydrochloric acid and 35 degrees of total acid. The cholangiograms were normal. A series of gastrointestinal roentgenograms revealed a filling defect arising from the posterior wall of the body of the stomach just below the cardia (figs. 1 and 2).

Gastroscopic examination revealed a polypoid lesion, about 1 inch (2.5 cm.) in size, high on the posterior wall of the stomach. The surface of the lesion was smooth. The remaining portions of the stomach showed an atrophic type of gastritis.

On June 6, 1950, an exploratory laparotomy was performed. A walnut-sized, firm, movable lesion was found on the posterior wall of the stomach in the fundic region. The lesion was attached to a narrow stalk. Immediately below the stalk was a firm, superficial ulcer of the stomach. This appeared oblong, and the edges were slightly elevated. No regional nodes were present.

A segmental resection of the lesion and ulcer was accomplished. Frozen sections were made but revealed no evidence of a malignant process. The defect in the stomach wall was closed. The patient's postoperative course was uneventful.

Pathological Examination.—The specimen from the stomach measured 5.5 by 4 cm. At one corner of the specimen was an ulcer which measured 3 cm. in length, 1.2 cm. in width and

Fig. 2.—Defect at point of arrow represents tumor on barium studies of the stomach.

Fig. 3.—Circumscribed tumor with mucosa inflamed but intact over the tumor. Below tumor and to the right is a benign gastric ulcer from which a block of tissue has been removed.

2 mm. in depth. The base of the ulcer appeared necrotic. At the upper portion of the ulcer was a mass which measured 2.5 cm. in diameter, within the wall of the stomach. The mass was round and showed no evidence of ulceration (fig. 3). On cut section the mass was light gray, circumscribed and firm.

Microscopic examination revealed a deep ulcer crater, with little remaining of the stomach wall. The mucosa stopped abruptly, and the edge was overhanging the ulcer (fig. 4). There

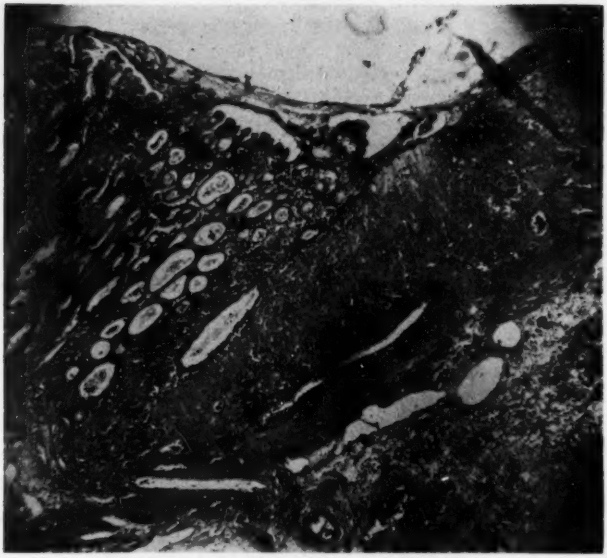

Fig. 4.—Section through gastric ulcer showing loss of mucosa and penetration into deeper layers of stomach wall on the right. The left shows the margin of the ulcer with intact but injected mucosa.

Fig. 5.—Section through the tumor showing intact mucosa above and twisted bundles of cells below. The nuclei have a palisading arrangement.

was some infiltration with neutrophils and eosinophils. A slight hemorrhage was present. No evidence of perforation or malignancy was found.

A section from the tumor revealed it to be encapsulated and made up of fibrous tissue, some of which showed hyalinization and spindle-shaped cells with long nuclei, which in some areas showed palisading (fig. 5).

Pathological Diagnosis.—The diagnosis was (1) benign ulcer of the stomach, and (2) neurofibroma of the stomach.

SUMMARY

A case of neurofibroma of the stomach with associated benign gastric ulcer which was located adjacent to the tumor has been presented. A brief review of the literature is given, and the main pathologic features are pointed out. The incidence, etiology, complications such as hemorrhage, pyloric obstruction and malignant changes are discussed. The treatment of choice is wide local excision or sleeve resection of the stomach if the lesion is benign. Gastric resection is indicated in cases in which there is doubt as to whether the tumor is benign or malignant.

LEIOMYOMA OF THE JEJUNUM

A Neoplasm Imitating the Symptoms of Duodenal Ulcer

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LEIOMYOMAS of the digestive tract are infrequently encountered, since many of them are asymptomatic and are incidental findings at autopsy or operation and consequently their symptoms are apt to be attributed to commoner ailments. The symptoms of leiomyoma are often those of duodenal ulcer, a common lesion, and it is only natural that the latter should receive preferential consideration in diagnosis. We recently observed a patient with epigastric pain, bleeding from the bowel and roentgen evidence of duodenal spasm and irregularity, which symptoms were incorrectly interpreted as being due to a duodenal ulcer. The patient was treated for an ulcer, on a conservative regimen, for several months, with incomplete relief, and an operation ultimately revealed a leiomyoma of the jejunum which had been the cause of the bleeding, pain and duodenal irregularity.

Segal, Scott and Watson [1] first directed attention to the impressive mimicry of this syndrome in 1945. They reported three lesions of the small intestine simulating duodenal ulcer and collected six more from the literature. They stated that "neither melena alone nor pain alone caused by lesions in the jejunum or ileum is too unusual. However, the combination of these two symptoms presenting a picture simulating peptic ulcer but produced by pathologic conditions in the small intestine beyond the duodenum has not been emphasized in the literature." This report listed various benign and malignant lesions in the small intestine, which have been observed to imitate the symptoms of duodenal ulcer. We have noted in our review that leiomyomas are oftenest the cause of this mimicry.

HISTORY AND INCIDENCE

The first authentic report of a leiomyoma occurring in the small intestine was by Foerster in 1858. King [2] in 1925 collected 43 myomatous tumors of the intestinal tract; 22 of these were in the small intestine. Raiford [3] in 1932 examined 11,500 autopsy reports and 45,000 surgical specimens at Johns Hopkins Hospital and

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1. Segal, H. L.; Scott, W. J. M., and Watson, J. S., Jr.: Lesions of the Small Intestine Producing Massive Hemorrhage, with Symptoms Simulating Peptic Ulcer, J. A. M. A. **129**:116 (Sept. 8) 1945.

2. King, E. L.: Benign Tumors of the Intestines with Special Reference to Fibroma, Surg., Gynec. & Obst. **25**:54 (July) 1917.

3. Raiford, T. S.: Tumors of the Small Intestine, Arch. Surg. **25**:122 (July) 1932; **25**:321 (Aug.) 1932.

found 88 neoplasms of the small bowel, three of them leiomyomas. Rankin and Newell [4] searched the files of the Mayo Clinic in 1933 and discovered 35 benign and 60 malignant tumors primary in the small bowel; 11 of the benign tumors were leiomyomas. Golden and Stout [5] in a comprehensive review of the literature in 1941 collected 197 cases of small intestinal leiomyomas. Since that time, sporadic case reports have increased the total number of reported cases to approximately 210.

MORPHOLOGY AND SYMPTOMATOLOGY

Leiomyomas are usually classified on the basis of relationship to layers of the bowel wall, as subserosal (fig. 1) or submucosal, according to whether they project out or in. The commonest surgical complications of leiomyomas are obstruction and hemorrhage. Perforation is rare. Obstruction occurs oftener in submucosal than in subserosal lesions because of intussusception or growth into the bowel lumen. Subserosal tumors produce obstruction, infrequently, by angulation or torsion.

The subserous leiomyomas may attain such size as to attract the attention of the patient or the physician.

Bleeding occurs with both types of tumors but by different mechanisms. Mucosal ulceration is the causative factor in bleeding from the submucosal variety. Subserosal tumors bleed, as Smith has clearly shown, by massive central necrosis, liquefaction and discharge of the contents into the lumen of the bowel, creating a pseudodiverticulum with persistent bleeding (fig. 3). It might be well to note that bleeding from jejunal leiomyomas produces melena; in no instance have we found reference to hematemesis. The latter could ensue but would entail a combination of obstruction and bleeding to explain the regurgitation of blood.

The subserosal variety has been reported to metastasize in 16 per cent of the cases, whereas the submucosal myoma is supposed rarely or never to become malignant. Criteria for establishing malignancy are based on metastasis or recurrences, or both, rather than on the unreliable histological pattern.

The obstructive type of pain produced by smooth muscle tumors of the small intestine offers no particular diagnostic difficulty. The ulcer-like pain occasionally present may lead to an error in diagnosis, particularly if associated with and abetted by the presence of other findings suggestive of the more commonly found duodenal ulcer.

We have collected from the literature eight cases in which the diagnosis of duodenal ulcer had been made because of a combination of abdominal pain, melena and sometimes roentgenographic evidence of duodenal irregularity and in each instance operation or autopsy revealed that a leiomyoma had been responsible for the symptoms. This mimicry is even more perplexing if one considers the fact that the diagnosis, although erroneous, had been made on a rational basis in each case.

CASE 1.—The patient of Klopp and Crawford [6] was a 45 year old woman whose chief complaint was of tarry stools and abdominal pain. Her roentgenograms were reported as being suggestive of duodenal ulcer. Operation was performed, and no ulcer was present, but there was found a leiomyoma of the jejunum. Resection of the lesion was followed by recovery.

4. Rankin, F. W., and Newell, C. S.: Benign Tumors of the Small Intestine: Report of 24 Cases, Surg., Gynec. & Obst. **57**:501 (Oct.) 1933.

5. Golden, T., and Stout, A. P.: Smooth Muscle Tumors of the Gastrointestinal Tract and Retroperitoneal Tissues, Surg., Gynec. & Obst. **73**:784 (Dec.) 1941.

6. Klopp, E. J., and Crawford, B. L.: Leiomyoma of Small Intestine, Ann. Surg. **101**:726 (Feb.) 1935.

CASE 2.—Smith [7] reported the case of a 58 year old man whose symptoms were upper abdominal pain and vomiting (no blood) associated with melena. The tentative diagnosis was duodenal ulcer. This patient succumbed from persistent hemorrhage. At autopsy a leiomyoma was discovered 220 cm. from the ileocecal valve.

CASE 3.—A 57 year old man, reported on by Klingenstein,[8] was treated for duodenal ulcers because of tarry stools, vertigo and syncope and a roentgenogram which reportedly revealed a duodenal ulcer. He suffered a recurrence, and again a roentgenogram showed duodenal irritability. Later a mass developed in his left upper quadrant. A leiomyoma of the ileum was found when laparotomy was performed. This patient had six hemorrhages over a four year period. Resection of the leiomyoma resulted in a cure.

CASE 4.—The most astounding case was that of Hanno and Mensh.[9] A 53 year old man had repeated bouts of melena and epigastric distress which was relieved by the intake of food and alkali. His roentgenograms were suggestive of a duodenal ulcer. A gastroenterostomy was performed, although no duodenal ulcer was seen at the time of operation. The patient finally died as a result of intestinal bleeding, and autopsy revealed a walnut-sized leiomyoma just 8 inches (20 cm.) distal to the gastroenterostomy stoma.

CASES 5 and 6.—Both these cases were reported by Smith, Good and Gray.[10] The first, that of a 41 year old woman, complained of abdominal distress and recurrent melena. Her distress was relieved by the intake of food and soda. Deformity of the duodenal bulb was seen in the roentgenograms and diagnosed as duodenal ulcer. An operation was performed, and a leiomyoma was removed from the terminal portion of the ileum.

The other case, reported by these men, was that of a 32 year old man whose complaints were belching, bloating and sour stomach relieved by the intake of soda. He also had melena. A roentgenogram showed a duodenal ulcer, and a gastrectomy was performed. Epigastric pain recurred one month postoperatively and roentgenograms at this time were interpreted as showing gastrojejunitis. The patient had pain and recurrent melena for two years, at the end of which time a second operation was performed and a leiomyoma was removed from the midileum. The patient recovered and was asymptomatic thereafter.

CASE 7.—Marshall and Welch [11] reported the case of a 53 year old woman with epigastric distress and tarry stools. Her discomfort was partially relieved by the intake of food, and a filling defect of the duodenum was seen on roentgenograms. She was treated on an ulcer regimen, and evidence of duodenal ulcer was seen on repeated fluoroscopy and roentgenographic studies. She had recurrent melena. Exploratory laparotomy revealed a leiomyoma of the jejunum 15 cm. from the ligament of Treitz.

CASE 8.—Stewart [12] reported the case of a 63 year old Caucasian suffering from melena and abdominal cramps. Roentgenograms showed a filling defect of the duodenum. Exploratory laparotomy revealed a normal stomach and duodenum. It was followed by vague indigestion and repeated intestinal hemorrhages. Operation revealed a leiomyoma 3 feet (91 cm.) from the duodenum.

To this series, we would like to add our own case report.

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7. Smith, O. N.: Leiomyoma of the Small Intestine with Report of a Case with Fatal Hemorrhage, Am. J. M. Sc. **194**:700 (Nov.) 1937.

8. Klingenstein, P.: Benign Neoplasms of the Small Intestine Complicated by Severe Hemorrhage: Report of 2 Cases; Operative Intervention and Recovery, J. Mt. Sinai Hosp. **4**:972 (March-April) 1938.

9. Hanno, H. A., and Mensh, M.: Leiomyoma of the Jejunum: Intermittent Melena of 14 Years Duration and Fatal Hemorrhage, Ann. Surg. **120**:199 (Aug.) 1944.

10. Smith, L. A.; Good, C. A., and Gray, H. K.: Tumor of the Small Intestine as the Cause of Recurrent Melena: Report of 2 Cases, Proc. Staff Meet., Mayo Clin. **19**:117 (March 8) 1944.

11. Marshall, S. F., and Welch, M. L.: Leiomyoma of Jejunum: Report of a Case, New England J. Med. **236**:95 (Jan. 16) 1947.

12. Stewart, J. B.: Tumor of the Small Intestine: Miller-Abbott Tube Determines Site of Massive Hemorrhage, Ann. Surg. **128**:299 (Aug.) 1948.

REPORT OF A CASE

M. A., a 44 year old Filipino, was admitted to the Queen's Hospital in 1947 with the chief complaint of tarry stools, epigastric pain, weakness and dizziness of 12 hours' duration. Generalized tenderness in the abdomen was the only noteworthy physical sign. The red blood cell count was 3,500,000 per cubic millimeter, and the hemoglobin content 8.5 Gm. per 100 cc. A gastrointestinal roentgenogram revealed an irritable and spastic duodenal bulb; this was interpreted by the roentgenologist as being consistent with the clinical diagnosis of duodenal ulcer.

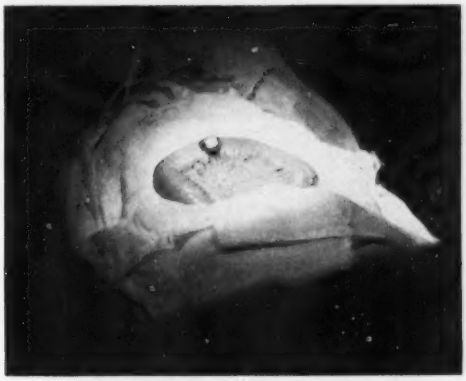

Fig. 1.—The appearance of the leiomyoma at the operating table. Note the antimesenteric location and the wedge-shaped area of enlarged glands in the mesentery. These glands revealed inflammatory hyperplasia as a result of the ulceration in the tumor.

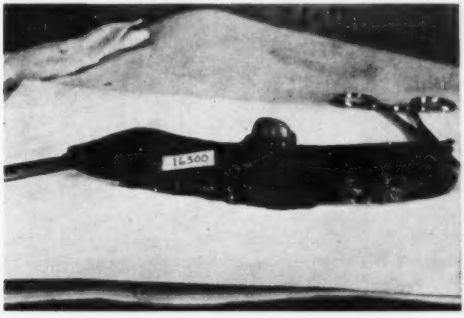

Fig. 2.—Close-up to reveal the serosal projection of the tumor. Bowel is unopened, and the resected mesentery with accompanying glands is visible at the lower border.

The bleeding abated, the patient rapidly regained his strength and he was discharged on Sept. 8, 1947, with instructions for following a medical and dietary regimen for peptic ulcer.

At the time of his admission, it was noted that the patient had been previously admitted in August 1944. His chief complaint at that time was of cramping pain in the left epigastrium. An appendectomy was performed and a normal appendix removed through a McBurney incision. His convalescence was rapid and uneventful, and there was no history of pain in the intervening years.

He was readmitted on Dec. 19, 1947, complaining of repeated black and dark red stools, pain in the epigastrium and progressive weakness. The hematocrit reading was 21 per cent and the hemoglobin content 5 Gm. per 100 cc. The patient was given a transfusion of several liters of citrated whole blood and prepared for surgical intervention.

On Dec. 31, 1947, a laparotomy was performed with the patient under intratracheal gas-ether anesthesia. Examination of the stomach and duodenum revealed those structures to be grossly normal. On examination of the small bowel there was found, about 35 cm. distal to the ligament of Treitz, a rubbery tumor the size and shape of the distal joint of a man's thumb (fig. 1). It had the appearance of a benign tumor, but there were several enlarged lymph nodes in the immediately adjacent segment of mesentery. A frozen section of one of the nodes was reported as showing inflammatory reaction only. That portion of the jejunum including approximately 12 cm. of normal intestine on each side of the tumor was resected along with a generous wedge of the gland-bearing mesentery, and an end to end jejunojejunostomy was accomplished with a double row of fine cotton sutures. The incision was closed, and the patient returned to the ward in good condition. The postoperative course was uneventful, and he was discharged on the twelfth postoperative day. He has remained asymptomatic for a period of two years.

Gross examination of the specimen showed approximately 20 cm. of small intestine, with a wedge-shaped area of mesentery within which were 15 to 20 enlarged lymph nodes. A well

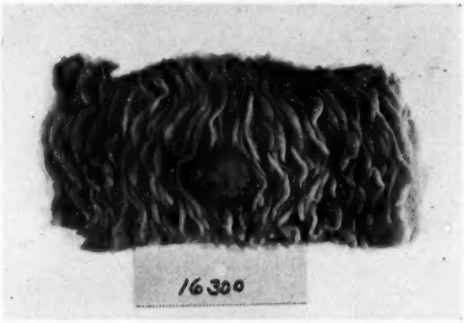

Fig. 3.—Mucosal view to show the ulcerated area communicating with a central cavity produced by necrosis. This was the source of the repeated episodes of hemorrhage.

defined tumor, rubbery, cylindrical and measuring 2 cm. in diameter and 4 cm. in length, occupied a position on the antimesenteric border of the center of the specimen (fig. 2). On section, the substance of the tumor was grayish pink and its fibers were arranged in whorls. The center was occupied by a cavity, 1.5 by 3 cm., which opened through a small aperture into the lumen of the intestine.

Histological examination of the tissue revealed a benign neoplasm composed of smooth muscle elements and showing marked vascularity. Examination of the accompanying lymph nodes showed a chronic inflammatory reaction and some obliteration of the follicular architecture but no evidence of metastatic tumor.

COMMENT

Since duodenal ulcers are 240 to 260 times as common as tumors of the small intestine, it is readily appreciated that they usually receive primary consideration in the search for a cause of melena and abdominal distress. If, as in many of the cases cited, roentgen evidence of duodenal irregularity and spasticity corroborates the other findings, then the incorrect diagnosis seems even more justified. Marshall and Welch have aptly stated that "the key to diagnosis of small bowel lesions is suspicion."

Various technics for roentgenographic demonstration of tumors of the small bowel have been described. It is the general consensus, however, that roentgen examinations rarely offer significant aid in their diagnosis unless the clinician is suspicious enough to alert the roentgenologist to the possible existence of such a lesion.

SUMMARY

Leiomyomas of the small intestine may produce a symptom complex closely resembling that of duodenal ulcer. In a number of cases, melena, epigastric distress and even suggestive roentgen findings have contributed to a diagnostic error. A submucosal leiomyoma may bleed from mucosal erosion but oftenest manifests symptoms by intussusception and obstruction. The subserosal variety may achieve such size as to attract attention to the mass; it bleeds by the formation of a pseudo-diverticulum, and it undergoes malignant degeneration in 16 per cent of cases. Special roentgen studies of the small intestine may demonstrate a tumor but rarely do so because the lesion is not often suspected and observation of the barium stream is therefore not sufficiently prolonged.

KELLER OPERATION FOR HALLUX VALGUS AND HALLUX RIGIDUS

An End Result Study

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THIS REPORT is based on the results of 161 Keller operations for hallux valgus and hallux rigidus on 100 patients [1] during a 12 year period (1935 to 1947). Resection of two thirds of the proximal phalanx of the great toe combined with "exostosectomy" of the head of the first metatarsal is our method of choice for treating the majority of patients with hallux valgus and hallux rigidus.

In addition, we wish to emphasize the need for attention to the disabilities and deformities of the foot invariably associated with hallux valgus if the patient is to obtain maximum benefit from any type of surgical treatment.

Although Keller [2] reported his method of resection of the proximal part of the proximal phalanx and removal of the medial aspect of the metatarsal head in 1904 and 1912,[3] the operation did not become popular until the past decade, in spite of Spiers's [4] favorable report in 1920 and that of Anderson [5] in 1929. Meanwhile, Brandes [6] popularized the operation in Europe, and in 1938 Galland and Jordan presented their technic and urged that the operation be used more widely.[7]

Since 1938, Haggart and Toumey,[8] Ober, [9] Schein,[10] Smith,[11] Starr,[12] McMurray,[13] Cleveland, Willien and Doran [14] and Nelson and Kaplan [15] have expressed preference for the Keller operation.

Drs. Galland, Wiesenthal and Gaynor gave permission for inclusion of their patients in this follow-up study.

1. Fifty-six per cent of the series were patients of the senior author; 18 per cent were those of Dr. S. S. Gaynor. The remaining 26 per cent were patients of the Orthopaedic Department, Lenox Hill Hospital, New York (service of Dr. W. I. Galland and Dr. A. Wiesenthal).

2. Keller, W. L.: Surgical Treatment of Bunions and Hallux Valgus, New York M. J. **80**:741-742, 1904.

3. Keller, W. L.: Further Observations on the Surgical Treatment of Hallux Valgusa Bunius, New York M. J. **95**:696 (April 6) 1912.

4. Spiers, H. W.: End-Result Study of Hallux Valgus Operations, J. A. M. A. **75**:306-307 (July 31) 1920.

5. Anderson, R. L.: Hallux Valgus: Report of End Results, South. Med. & Surg. **91**:74-78 (Feb.) 1929.

6. Brandes, M.: Zur operativen Therapie des Hallux valgus, Zentralbl. f. Chir. **56**:2434-2440 (Sept. 28) 1929.

7. Galland, W. I., and Jordan, H. H.: Hallux Valgus, Surg., Gynec. & Obst. **66**:95-99 (Jan.) 1938.

8. Haggart, G. E., and Toumey, J. W.: Surgical Correction of Hallux Valgus with Dorsal and Medial Exostoses, S. Clin. North America **19**:721-725 (June) 1939.

END RESULTS

The classification of our 100 patients is presented in table 1, and the end results are recorded in table 2.

Among 161 Keller operations a result satisfactory to both patient and surgeon was obtained in 159, or 98.7 per cent. The two unsatisfactory results (partial ankylosis and pain in the first metatarsophalangeal joint) are due to removal of

TABLE 1.—*Classification of One Hundred Patients Who Underwent 161 Operations (Ninety-Three Women and Seven Men)*

Age, yr. (at time of surgical treatment)	Occupation (as recorded in 70 patients)
No. past 50 62	"Standing" 67%
No. past 60 30	"Sedentary" 33%
No. past 70 ..... 3 (oldest 76 yr.)	
Average age 51	

Diagnosis	Total	Unilateral	Bilateral
Hallux valgus	80	20	60
Hallux rigidus	12	11	1
Hallux valgus rigidus	7	7	..
Hallux rigidus varus	1	1	..
Foot deformities (in addition to or responsible for hallux valgus or hallux rigidus)			
Pes valgus or planovalgus of varying degrees	98	..	..
Transversoplanus with metatarsalgia	36	..	..
Dorsal displacement 2d toe	17	..	(3)
One or several hammer toes	16	..	(5)
Digitus quintus varus	4	..	(2)
Spastic flat foot	3	..	..
So-called dorsal exostosis (degenerative arthritis of first metatarsocuneiform joint with dorsal osteophyte)	3	..	..

Recurrence after previous surgical treatment (9 patients [12 operations])

Type of operation:

Simple exostosectomy	5
Mayo	2
Bursectomy	2
Silver	1
Keller (bilateral, insufficient bone removed)	2
Average hospital stay	15 days

Postoperative follow-up observation, yr.

More than 10	10
More than 5	46
Less than 2	25
Average, 3½	

9. Ober, F. R., in discussion on Jones, E. A.: McBride Operation for Hallux Valgus, Tr. New England S. Society **23**:57-60, 1941.

10. Schein, A. J.: Keller Operation: Partial Phalangectomy in Hallux Valgus and Hallux Rigidus; 55 Operations in 32 Cases, Surgery **7**:342-355 (March) 1940.

11. Smith, P. E.: Hallux Valgus: A Consideration of the Keller-Brandes Operation, Mississippi Doctor **20**:445-450 (March) 1943.

12. Starr, D. E.: The Keller Operation, Bull. Vancouver M. A. **18**:301-330 (July) 1942.

13. McMurray, P. T.: Treatment of Hallux Valgus and Rigidus, Brit. M. J. **2**:218-221 (Aug. 1) 1936.

14. Cleveland, M.; Willien, L. J., and Doran, P. C.: Surgical Treatment of Hallux Valgus in Troops in Training at Fort Jackson During Year of 1942, J. Bone & Joint Surg. **26**:531-534 (July) 1944.

15. Nelson, L. S., and Kaplan, E. B.: Hallux Valgus: Survey of End Results of Various Operative Procedures for Correction of Hallux Valgus Performed at the Hospital During Past 10 Years (1931-1940), Bull. Hosp. Joint Dis. **3**:17-25 (Jan.) 1942.

insufficient proximal phalanx (fig. 4). In evaluating the end results one must remember that the operation is designed to correct the deformity and symptoms of hallux valgus or hallux rigidus and that it has no direct influence on preexisting foot pronation or on coexisting deformities (viz., hammer toes, metatarsalgia with displacement of proximal phalanges onto the dorsum of the metatarsal heads).

In table 1 it may be noted that associated pathological conditions of the foot were found in all but two of the 100 patients (two cases of unilateral hallux rigidus due to rheumatoid arthritis).

In all cases relief was sought because of pain and not for cosmetic reasons alone. In every patient the hallux valgus or hallux rigidus had been present more than five years.

The average follow-up period was three and one-half years and in no case less than one year. Ten patients have been followed for more than 10 years and 46 for more than five years.

Nine patients had had previous surgical treatment for bunions (five exostosectomies in three patients; two Mayo operations; two bursectomies; one Silver

TABLE 2.—*Tabulation of Postoperative Results (Functional and Cosmetic)*

		No. of Cases	No. of Operations
Excellent 90%	No pain; no deformity; good function of great toe	86.5	145
Good 8.7%	No pain; slight residual deformity (5) or dorsiflexion contracture (7) but good function of great toe	12	14
Poor 1.3%	Recurrence of pain and disability with deformity and limitation of motion	1.5	2
		100	161
Summary		% Patients	% Operations
End results satisfactory to both patient and physician		98.5	98.7

operation resulting in a rigid hallux varus, and one bilateral Keller operation, in which insufficient removal of the proximal phalanx resulted in incomplete correction of the deformity and pain in the first metatarsophalangeal joint).

The average period before return to work was five weeks. Convalescence was no more prolonged after a bilateral operation than after unilateral operation but seemed to depend chiefly on the arduousness of occupation and the economic need of the patient. However, full mobility and maximal function did not accrue in most patients for several months.

ETIOLOGICAL ASPECTS

The causation of hallux valgus is still a matter of controversy between those who believe that it is due to a congenital or "primary" varus of the first metatarsal and those who, like ourselves, attribute it to the deforming mechanical influence of foot pronation. Although this dispute is to some extent academic, our concepts are presented because they constitute the basis for successful therapy of hallux valgus and rigidus.

On rare occasions a child may be born with a fixed hallux valgus deformity,[16] and less rarely hallux valgus may develop as the result of uncorrected congenital

16. Heller, E. P.: Congenital Bilateral Hallux Valgus, Ann. Surg. **88**:798-800 (Oct.) 1928.

metatarsus varus.[17] We regard the majority of cases of hallux valgus and hallux rigidus as acquired deformities resulting from foot pronation. The role of footwear is secondary, serving to aggravate an existing mild deformity or to produce manifest deformity where only potential hallux valgus previously existed as a result of foot pronation. Rogers,[18] Hauser,[19] Ober,[9] Haggart,[8] Silver,[20] Hiss,[21] Armstrong [22] and Anderson [5] similarly emphasize the importance of pes plano valgus and urge correction of foot deformities as part of the management of hallux valgus.

We visualize the mechanism of development of hallux valgus and hallux rigidus as follows: In pes plano valgus, locomotion occurs with the tarsus in pronation and the forefoot in supination causing increased weight-bearing thrust through the first metatarsal bone and the great toe. As a result of abnormal stress on the first metatarsophalangeal articulation, the great toe is forced laterally (hallux valgus). This is increased by the lateral thrust on the medial side of the toe as the everted foot pushes off. Instead of lateral displacement the articular cartilage of the first metatarsophalangeal joint may be worn down by excess weight bearing through the line of the great toe, producing a hallux rigidus (degenerative arthritis) with pain, limitation of motion and eventually flexion contracture. A compensatory hypermobility of the interphalangeal joint develops, with a callosity on the plantar aspect of the toe at this joint. The Keller procedure is also effective for ankylosing arthritis of the first metatarsophalangeal joint due to rheumatoid arthritis or suppurative arthritis. Short, narrow, pointed shoes and short stockings are prone to accentuate the lateral thrust on the great toe, and friction and pressure of the shoe over the medial prominence of the first metatarsal head produce pain and a bursa.

Of course, not all severely pronated feet develop hallux valgus or hallux rigidus. The higher incidence in women (93 per cent in our series) is explained by the fashion of women's shoes as contrasted with the better design of most men's shoes. The high heel, especially without a cupped heel seat, causes excessive weight bearing on the metatarsal heads, and in pes valgus much of this abnormal weight is shifted to the big toe. Development of deformity in these circumstances depends also on such constitutional factors as the tensile strength of the ligaments, the vitality of the cartilage and of the connective tissue in general and the elasticity of the gait, in short, on individual ability to resist the deforming forces and to recuperate from them.

Whether hallux valgus is acquired or congenital, results of the Keller operation indicate that it is rarely necessary to correct the position of the first metatarsal by

17. McCormick, D. W., and Blount, W. P.: Metatarsus Adductovarus: "Skewfoot," J. A. M. A. **141**:449-453 (Oct. 15) 1949.

18. Rogers, W. A., and Joplin, R. J.: Hallux Valgus, Weakfoot, and the Keller Operation: An End-Result Study, S. Clin. North America **27**:1295-1302 (Oct.) 1947.

19. Hauser, E. D. W.: Hallux Valgus, Hammer Toe, and Contracted Toes: Plastic Reconstruction and Ablation, S. Clin. North America **21**:169-180 (Feb.) 1941.

20. Silver, D.: Operative Treatment of Hallux Valgus, J. Bone & Joint Surg. **5**:225-232 (April) 1923.

21. Hiss, J. M.: Hallux Valgus: Its Cause and Simplified Treatment, Am. J. Surg. **11**:51-57 (Jan.) 1931.

22. Armstrong, W. P., Jr.: Treatment of Hallux Valgus, Am. J. Surg. **36**:332-338 (April) 1937.

osteotomy, wedge resection or fusion of the metatarsocuneiform joints.[23] Manual pronation of the first metatarsal and transverse compression of the metatarsus by circular strapping will in most cases adequately correct the metatarsus varus. Even when this correction has been neglected the Keller operation has provided a good functional result.

PATHOLOGIC CHANGES

The pathologic changes found in hallux valgus and hallux rigidus are essentially those of a traumatic osteoarthritis of the first metatarsophalangeal joint. This is most marked in hallux rigidus but is present to some degree in every hallux valgus of long standing.

Thus, one finds, in varying degree, narrowing of the joint space, fibrillation and erosion of articular cartilage, sclerosis of the subchondral bony plate, meta-

Fig. 1.—Illustrating the pathology of hallux valgus in a 56 year old woman. There is degenerative arthritis of both first metatarsophalangeal joints, with narrowing of the joint space, marginal lipping and sclerosis of the subchondral bony plates of the contiguous articular surfaces. The metatarsal heads are enlarged in all diameters in the same manner as the head of the femur in malum coxae senilis. The bared medial portions of the heads which no longer articulate with the bases of the proximal phalanges represent the "exostoses." The location of the deep groove in the articular cartilage of the metatarsal head, demarcating the "exostosis," is indicated by a slight indentation in the subchondral bone of the right first metatarsal head. There is dorsal dislocation of the proximal phalanx of the left second toe, with extension contracture of the metatarsophalangeal joint.

physial fibrosis or "fibrous cysts" in the head of the first metatarsal and osteophyte formation.

The medial prominence of the metatarsal head in hallux valgus is usually referred to as an "exostosis." However, examination of the "exostosis" in pre-

23. Kleinberg, S.: Operative Cure of Hallux Valgus and Bunions, Am. J. Surg. **15**:75-81 (Jan.) 1932. Lapidus, P. W.: Operative Correction of Metatarsus Varus Primus in Hallux Valgus, Surg., Gynec. & Obst. **58**:183-191 (Feb.) 1934. Peabody, C. W.: Surgical Cure of Hallux Valgus, J. Bone & Joint Surg. **13**:273-282 (April) 1931. Truslow, W.: Metatarsus Primus Varus or Hallux Valgus? ibid. **7**:98-108 (Jan.) 1925.

operative roentgenograms, at the time of operation and in a number of intact specimens removed at autopsy indicates that there is no true bony overgrowth of the head, except for a small exostosis often found on the neck of the metatarsal at the point of capsular attachment and moderate diffuse enlargement of the metatarsal head due to osteoarthritis. The appearance of an exostosis is simulated by the presence of a sharp groove in the articular cartilage separating a larger lateral articular surface from a smaller medial surface covered by articular cartilage and often referred to as the "exostosis." Stein [24] also regarded "exostosis" as a misnomer and felt, as we do, that it is merely an unduly prominent metatarsal head due to adduction of the metatarsal and abduction of the big toe. We believe that the groove in the head is due to pressure of the sharp medial edge of the base of the proximal phalanx. Therefore, the "exostosis" may be regarded as the medial part of the enlarged metatarsal head which has become prominent, since it no longer articulates with the phalanx (see fig. 1).

TECHNIC

The technic of the Keller operation was presented in detail by Galland and Jordan.[7] After removal of two thirds of the proximal phalanx it is easy to remove the "exostosis" and osteophytes with a sharp osteotome. It is often advisable to bevel sharp edges, especially the medioplantar edge.

As a rule we do not excise the "bursa" because it disappears after elimination of the bony prominence and of shoe pressure. If a large mass of fibrotic tissue is encountered at the site of a previously infected "bursa," it should be excised.

If the sesamoid bones show marked enlargement and deformity or if they have been the site of well localized pain, they can be removed easily after resection of the proximal phalanx, but we have rarely found this necessary.

Before closing the wound one should be certain that all extensor and flexor tendon tension has disappeared. The toe should be "floppy." If this is not the case after the removal of at least two thirds of the proximal phalanx, as in rare instances of a severe degree of hallux valgus, it is advisable to lengthen or section the extensor tendon proximal to the metatarsophalangeal joint. Longitudinal traction is applied to the great toe, by means of a heavy silk suture passed through the pulp and attached by a rubber band to an "outrigger" wire in the plaster boot. Elastic traction on the great toe gives a better scar and maintains the new joint space during organization of the hematoma. It is chiefly for the sake of elastic traction that we prefer to apply a plaster boot.

Cast, traction and sutures are usually removed on the tenth postoperative day. A firm cruricast® or elastoplast® circular strapping is applied from the toes to just below the knee, with transverse compression of the metatarsals. The patient may now be ambulatory, wearing low-heeled shoes with the medial one half of the toe cap removed. The foot of the bed remains elevated, for many weeks if necessary, and the circular strapping is changed at weekly intervals. Plaster of paris models for foot plates are made as soon as all swelling has subsided.

As pointed out above, the Keller operation corrects the hallux deformity, but it is not designed to correct the faulty static alinement of a pronated foot. If the valgus position dominates the picture, the original Whitman type foot brace is the appliance of choice. In the presence of transversoplanus with metatarsalgia and

24. Stein, H. C.: Hallux Valgus, Surg., Gynec. & Obst. **66**:889-898 (May) 1938.

for the more rigid foot, a plastic foot plate with lateral border is preferred.[25] Strapping should be continued until foot plates and new shoes are obtained.

How long foot plates and reasonable shoes (oxfords with 1½ to 1¾ inch [4 to 4.5 cm.] heels for women) should be worn depends on the individual case. The average patient should be limited to foot plates and oxfords for the first three months after the operation. Then it is often permissible to wear other shoes without support for social occasions. Four to six months postoperatively many patients are independent of foot plates and special shoes as far as the Keller operation is concerned. Fifty-four per cent of our patients discarded their orthopedic appliances after six months. The others have required continued use of foot plates and oxfords for working hours, because of residual symptoms due to pes plano valgus or metatarsalgia.

Some patients may become disturbed by the temporary "floppiness" of the great toe. It is therefore advisable to explain, prior to operation, that the great toe will be permanently shortened and that there will be a temporary loss of voluntary control of the hallux until postoperative adaptation occurs. The functional result will be the better the greater the immediate postoperative "floppiness" of the great toe.

The Keller operation is our procedure of choice for hallux valgus and hallux rigidus. Even the milder degree of hallux valgus requiring surgical treatment should have the benefit of the Keller operation. While exostosectomy may often give prolonged relief,[26] especially if foot pronation is corrected, it fails to correct the basic deformity and does not attack the osteoarthritis. Four of the patients in this series required Keller operations after previous exostosectomy.

The Keller operation is our procedure of choice because it is simple, safe and efficient in securing permanent correction of deformity and relief of bunion pain provided two thirds of the proximal phalanx is resected. It entails no greater surgical risk or postoperative disability than simple exostosectomy or any other method. Symptoms, such as metatarsalgia, pain over the scaphoid region or chronic strain of leg muscles may detract from the postoperative result, unless correct weight-bearing alinement of the lower extremity is restored and maintained by means of adequate orthopedic appliances and reasonable shoes.

Patients seek surgical treatment for relief of pain or for cosmetic improvement. The best subjects are those who desire an operation because of disability. One

25. Jordan, H. H.: Orthopedic Appliances: The Principles and Practice of Brace Construction for the Use of Orthopedic Surgeons and Bracemakers, New York, Oxford University Press, 1938; Foot Problems in Wartime, Arch. Phys. Therapy **24**:525-535 (Sept.) 1943.

26. Cleveland, M.: Hallux Valgus: Final Results in 200 Operations, Arch. Surg. **14**:1125-1135 (June) 1927. Levine, M. A.: An Operative Technique for Hallux Valgus, J. Bone & Joint Surg. **20**:923-924 (Oct.) 1938. McBride, E. D.: Surgical Treatment of Hallux Valgus Bunion, Am. J. Surg. **44**:320-321 (April) 1939; A Conservative Operation for Bunions, J. Bone & Joint Surg. **10**:735-739 (Oct.) 1928; The Conservative Operation for "Bunions," J. A. M. A. **105**:1164-1168 (Oct. 12) 1935. McElvenny, R. T., and Thompson, F. R.: Clinical Study of 100 Patients Subjected to Simple Exostosectomy for Relief of Bunion Pain, J. Bone & Joint Surg. **22**:942-951 (Oct.) 1940. McElvenny, R. T.: A Study of Hallux Valgus: Its Cause and Operative Management, Quart. Bull. Northwestern Univ. M. School **18**:286-297 (Winter Quarter) 1944; The Silver Procedure, Bull. Northwestern Univ. M. School **19**:23-31 (Spring Quarter) 1945; The Lapidus Operation, Bull. Northwestern Univ. M. School **19**:94-101 (Summer Quarter) 1945.

must be circumspect about patients who are interested solely in cosmesis, being sure to explain that the great toe may appear short and plump and that full voluntary control of the toe does not return for several months.

Although the Keller operation has no direct influence on preexisting foot or on coexisting deformities, 98 patients of this series of 100 experienced at least considerable relief of their associated disabilities and 28 per cent of them were completely asymptomatic at the time of follow-up examination.

Metatarsalgia is a complication which deserves serious consideration. It should be anticipated and its treatment planned preoperatively. Roentgenograms may show partial or complete dislocation of the proximal phalanx onto the dorsum of the head of the metatarsal, with depression of the metatarsal head and plantar callosity and pain. The second metatarsophalangeal joint is more frequently dislocated than the third or fourth (figs. 1, 2 and 4). We resect the proximal two thirds of the proximal phalanx of the affected toe, or the entire proximal phalanx

Fig. 2.—*A*, preoperative right hallux valgus and dorsolateral dislocation of the second toe in a 55 year old woman. *B*, ten months after Keller operation and removal of two thirds of the second proximal phalanx. Hallux valgus is corrected but second toe metatarsalgia persisted. *C*, nineteen months after removal of the distal third of the second metatarsal because of pain in the second toe. The foot is now asymptomatic. This patient returned the following year for a Keller operation on the left foot.

if the toe is a hammer toe. In one case it was necessary to resect the proximal portions of the second, third and fourth proximal phalanges.

While metatarsalgia constituted a preoperative complaint in 36 per cent of our patients, only 15 per cent had such pain postoperatively which was not relieved by routine postoperative management. In three of these patients, march fracture of the second metatarsal (detected about three months after operation) was responsible for the pain, subsiding after healing of the fracture. All three patients were past 40, were overweight and had severe foot pronation (fig. 3).

Although the Keller operation is experiencing increasing popularity, we feel that insufficient emphasis has been given to the amount of the proximal phalanx that should be removed for optimal results. Correction of the deformity occurs chiefly by shortening of the skeleton of the great toe, aided by release of the contracted lateral capsule and adductor hallucis tendon from their attachment to the

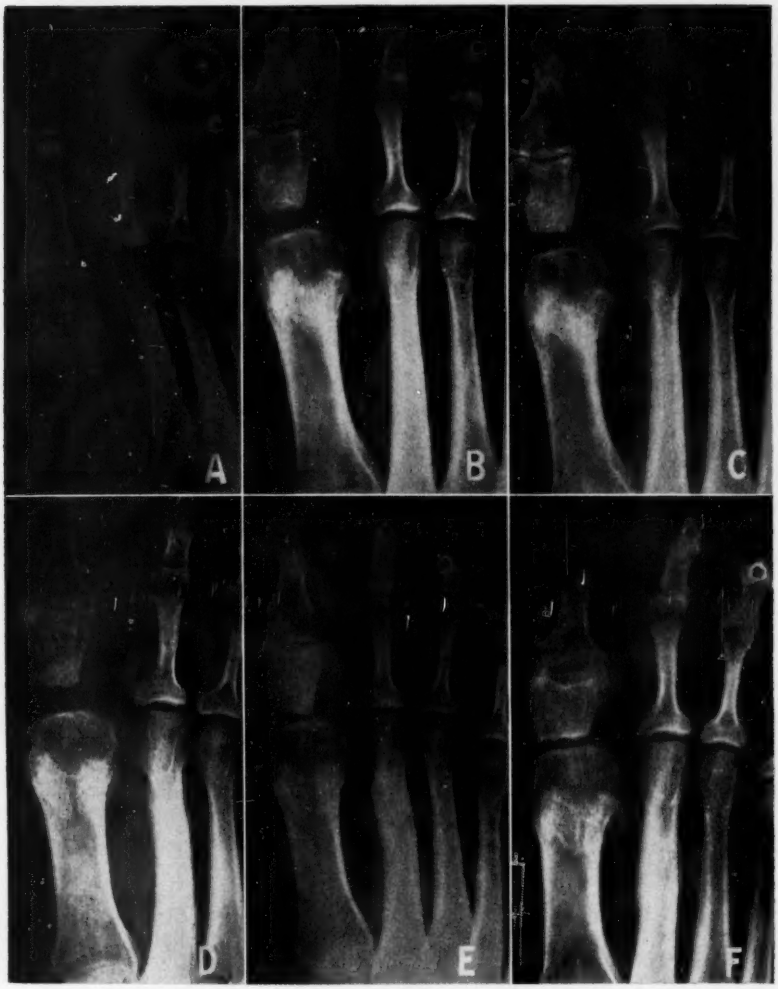

Fig. 3.—*A*, right hallux rigidus in a 40 year old woman. *B*, nine months after Keller operation patient complains of second toe metatarsalgia but roentgenogram fails to reveal pathologic changes. *C*, ten days later, second toe pain has become severer, and for the first time roentgenogram reveals periosteal new bone formation on the medial aspect of the neck of the second metatarsal, indicating a fatigue fracture. *D*, twelve months postoperatively the entire shaft of the second metatarsal is thickened and irregular. *E*, two years postoperatively patient's second toe symptoms are almost completely relieved with celluloid foot plates, but the roentgenogram shows persistence of second metatarsal thickening. *F*, three years postoperatively patient no longer has pain in second toe but there is residual cortical thickening.

base of the proximal phalanx. A new and larger joint space is created, substituting fibrous tissue for the articular surface of the proximal phalanx. While removal of less than two thirds of the proximal phalanx may permit correction of the average deformity, it does not allow correction of the higher degrees of valgus and often results in recurrence of deformity and limitation of motion.

Fig. 4.—*A*, preoperative (right) view of moderate hallux valgus in a 52 year old woman. *B*, and *C*, postoperative (right) view after Keller operation; an excellent result was obtained. *D*, left foot preoperatively. *E* and *F*, postoperative (left) view. After inadequate removal of proximal phalanx there is persistence of pain and limitation of motion. The bilateral dislocation of the second toe was treated simultaneously by resection of the entire proximal phalanx of the right and half of the phalanx on the left.

In the five patients in this series (six feet) whose results were classified as "good" because of mild persistent or recurrent hallux valgus, less than two thirds of the proximal phalanx was removed. Another patient required a second bilateral

Keller operation after nine years, with removal of an additional half of the proximal phalanx, because of recurrent valgus, pain and limited motion. We have seen a number of other patients in whom insufficient removal had resulted in recurrence of varying degrees of hallux valgus and/or hallux rigidus (fig. 4).

Recently Rogers and Joplin [18] concluded that while the operation was effective in relieving great toe pain and in permitting easier fitting of shoes it failed to help associated abnormalities, especially metatarsalgia and phalangeal contractures. They also stated that the operation fails to restore the power of the great toe lost through deformity and that it does not arrest the progress of degenerative arthritis of the joint. We agree with their emphasis on the high incidence and significance of associated changes. In our experience, however, the Keller operation imposes no additional burden on the foot, nor is it followed by loss of power or function of the great toe. On the contrary, our study would indicate that the Keller operation facilitates correction of residual foot deformities by permitting the use of adequate orthopedic appliances and shoes. The three instances of postoperative fatigue fracture of the second metatarsal, however, indicate an abnormal strain on this bone, which we have interpreted as an involuntary attempt on the patient's part to avoid bearing full weight on the great toe operated on. In each of these patients the fractures healed and the metatarsal pain cleared up after normal weight-bearing stance and gait had developed. After three to six months, the majority of our patients gained a greater range of motion and better power than they had had prior to surgical intervention.

CONCLUSIONS

The highest percentage of permanent end results satisfactory to patient and surgeon alike will be obtained by the Keller operation for hallux valgus or hallux rigidus, in preference to any other method, provided at least two thirds of the proximal phalanx is removed, the extensor tendon is lengthened whenever necessary, coexisting deformities of other toes are corrected by simultaneous operation and, finally, painstaking attention is given to postoperative lateral compression of the metatarsus and to after-care with corrective orthopedic appliances to be worn in well fitting shoes.

Case Reports

CYSTIC DILATATION OF THE COMMON BILE DUCT

E. LEE STROHL, M.D.
AND
FRANCIS E. SARVER, M.D.
CHICAGO

IT IS NOW 227 years since cystic dilatation of the common bile duct was reported by Vater.[1] Since that time about 185 [2] cases have been reported. Judd and Greene [3] state that one cyst of the common bile duct was found in 17,381 operations on the biliary tract. Many methods for the correction of this condition have been used.[4] This report deals with the successful treatment of a cystic dilatation of the comomn bile duct by a Roux en Y anastomosis between the cystic dilatation and the jejunum. This patient has been followed for a period of two years. Furthermore, a normal pregnancy and delivery have occurred since the operation.

REPORT OF CASE

P. F., a 24 year old white housewife, was admitted to St. Luke's Hospital, Chicago, on Jan. 13, 1948. The history revealed episodes of right upper quadrant pain, nausea and vomiting.

Read at the meeting of the Chicago Surgical Society on May 5, 1950, Chicago.

From the Departments of Surgery, St. Luke's Hospital and the University of Illinois College of Medicine.

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2. (*a*) Bremer, J. L.: Diverticula and Duplications of the Intestinal Tract, Arch. Path. **38**:132-140 (Sept.) 1944. (*b*) Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941, chap. 21. (*c*) McLaughlin, E. F.: Choledochus Cyst, Ann Surg. **123**:1047-1062 (June) 1946. (*d*) McWhorter, G. L.: Congenital Cystic Dilatation of the Common Bile Duct, Arch. Surg. **8**:604-626 (March) 1924. (*e*) Shallow, T. A.; Eger, S. A., and Wagner, F. B., Jr.: Congenital Cystic Dilatation of the Common Bile Duct: Follow-Up on Previously Reported Case and Report of Additional Case, Ann. Surg. **123**:119-126 (Jan.) 1946. (*f*) Swartley, W. B.: Choledochus Cyst: Final Report of 2 Cases, ibid. **118**:91-96 (July) 1943. (*g*) Swartley, W. B., and Weeder, S. D.: Choledochus Cyst with a Double Common Bile Duct, ibid. **101**:912-920 (March) 1935. (*h*) Zinninger, M. M., and Cash, J. R.: Congenital Cystic Dilatation of the Common Bile Duct: Report of a Case and Review of the Literature, Arch. Surg. **24**:77-105 (Jan.) 1932. (*i*) Weeder, S. D.: Choledochus Cyst with a Double Common Bile Duct: Sequelae and Complications, Ann. Surg. **110**:55-59 (July) 1939. (*j*) Winterstein, O.: Bile Duct Cysts: Diagnosis, Wien. med. Wchnschr. **82**:638-639 (May 21) 1932. (*k*) Yotuyanagi, S.: Contribution to the Etiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile Duct With Report of 3 Cases: New Etiological Theory Based on Supposed Unequal Epithelial Proliferation at Stage of Physiological Epithelial Occlusion of Primitive Choledochus, Gann. **30**:601-650 (Oct.) 1936. (*l*) Zollinger, R: A Method of Valvular Cholecystgastrostomy, Surg., Gynec. & Obst. **70**:71-78 (Jan.) 1940. (*m*) Shallow, T. A.; Eger, S. A., and Wagner, F. B., Jr.: Congenital Cystic Dilatation of the Common Bile Duct: Case Report and Review of Literature, Ann. Surg. **117**:355-368 (March) 1943.

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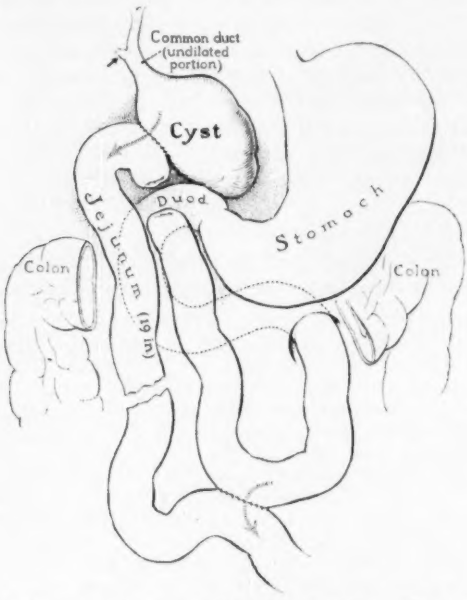
dating from childhood. The mother stated that the patient had the first episode at the age of two years. The syndrome of pain, nausea and vomiting seemed to be associated with emotional stress and nervousness. When the patient was a child, the attacks were relieved by the administration of opium suppositories and barbiturates rectally. For a number of years the patient had relied on these medications for relief.

On Jan. 7, 1948, the patient had an attack of severe pain in the right upper quadrant, with nausea and vomiting. The nausea and vomiting persisted after the relief of pain.

Physical examination revealed a well developed, well nourished white woman in severe pain, with the thighs flexed on the abdomen. There was low grade jaundice. The blood pressure was 130/90 mm. of mercury. The rectal temperature was 100.4 F. The general physical examination revealed no abnormalities except for deep tenderness in the right upper



Method of anastomosis between the cystic dilatation and the jejunum.

quadrant. The only significant laboratory findings were a slow direct qualitative van den Bergh reaction and an icteric index of 10 units. All other data were within normal limits.

The jaundice and temperature subsided promptly. Cholecystograms, with the oral, the double oral and the intravenous method, revealed no visualization of the gallbladder.

On March 2, 1948, an operation had been performed which revealed a small contracted gallbladder, with no evidence of stones. There was pronounced dilatation of the common bile duct. When the duct was opened, there was an escape of normal-appearing bile. No stones were present. A T tube had been inserted into the duct, and the gallbladder was removed at that time.

The patient came under our observation with the T tube in place, draining between 300 and 1,000 cc. of bile daily. The bile had been replaced into the gastrointestinal tract by daily gastric intubation. After the insertion of the T tube in March 1948 there had been no recurrence of right upper quadrant pain, nausea or vomiting.

A cholangiogram revealed an enormous dilatation of the common bile duct. It was our opinion that we were dealing with a cystic dilatation of the congenital type.

Operation.—On June 11, 1948, with the patient under general anesthesia, the abdomen was opened through a right upper quadrant incision. The T tube was traced to its entrance into the common duct, which was enormously dilated. The dilatation was such that it had the appearance of a gallbladder although this organ had been removed previously. The stump of the cystic duct was identified. Exploration revealed no stones. A probe passed easily into the right and left hepatic ducts and into the duodenum. The caliber of this cystic dilatation was the same as that of the small bowel. We elected to anastomose between the dilatation and the jejunum rather than attempt resection (figure). A loop of jejunum was brought up through the transverse mesocolon to the cystic dilatation, and a side to side anastomosis was made between the wall of the latter and the jejunum. An enteroenterostomy was made 19 inches (48 cm.) distal to the new bile outlet. The jejunum was transected just proximal to the anastomosis between the cystic dilatation and the jejunum. The cut ends were then inverted. One Penrose drain was inserted in Morison's pouch. The postoperative course was uneventful, and the patient left the hospital on the tenth postoperative day.

COMMENT

Cystic dilatation of the comon duct is a rare condition which should be recognized and corrected at the time of surgical intervention. An accurate preoperative diagnosis is made rarely.[5] The clinical manifestations of abdominal pain, mass and jaundice have been noted frequently. This triad of symptoms should lead one to think of the disease, as pointed out by Shallow [2e] and Gross.[6] Of 185 cases studied by Shallow, 77 per cent presented an abdominal mass, 70 per cent jaundice and 59 per cent pain.

When the condition of cystic dilatation of the common bile duct is recognized, corrective measures should be directed toward establishing a free flow of bile from the dilatation into the gastrointestinal tract. The anastomosis should be one which prevents regurgitation of intestinal contents into the biliary tree. Cole[7] states that the intestinal contents will ascend for a distance of 12 to 15 inches (30 to 38 cm.). It is for these reasons that we elected to use the Roux principle for establishing the anastomosis. The new bile outlet was about 19 inches (48 cm.) above the enteroenterostomy. A further technical advantage of this type of anastomosis is that there is no sacrifice of the blood supply of the loop of bowel which is anastomosed to the cystic dilatation of the common duct.

On Feb. 27, 1949, the patient was admitted to St. Luke's Hospital for laboratory studies. Roentgen studies of the upper gastrointestinal tract revealed no evidence of reflex of barium sulfate into the biliary tree. All laboratory data were within normal limits.

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The patient has been observed postoperatively for two years. She has remained in excellent health and has recently completed a normal pregnancy without complication.

SUMMARY

A report of a case of cystic dilatation of the common bile duct is presented. A Roux en Y anastomosis was made between the cystic dilatation and a common bile duct. The patient had had a normal pregnancy and delivery after surgical treatment and has been followed for a period of two years, with no recurrence of her preoperative symptoms.

122 South Michigan Avenue.

POSSIBLE ETIOLOGICAL FACTOR IN A PHARYNGOESOPHAGEAL DIVERTICULUM

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NEWPORT NEWS, VA.

THE SUBJECT of pharyngoesophageal diverticulum is an interesting one, not because the diverticula are rare but because the etiological factors are not definitely known. Most of the authors, including Lahey [1] and Harrington,[2] feel that there is a true herniation of the mucosa and submucosa of the esophagus, probably resulting from a congenital weakness plus the pulsion force of swallowing which causes the herniation. King [3] also states that herniation of the esophageal wall may result from pressure of the lower border of the cricoid cartilage against the ridge of the fifth cervical vertebral joint. Bortone [4] shows that the pouch usually arises just above the beginning of the esophagus and bulges through the cricoid-pharyngeal muscle and the herniation probably results from mechanical pressure. Scott [5] feels that it is a congenital anomaly in which repeated pressure on a weak area loosens the attachment of the cricopharyngeal muscle and results in a diverticulum. Kulvin [6] reports five cases, in one of which there was an esophageal stenosis due to a lye burn, followed by a diverticulum. From the foregoing, it is apparent that the cause of an esophageal diverticulum is not entirely understood, and the following case is being reported because of the fact that the immediate etiological factor, as far as can be determined, was increased air pressure in the mouth and pharynx, the increase in pressure resulting from a blast of air at 300 pound (136 Kg.) pressure.

The patient, a 59 year old white engineering mechanic, was first seen on Sept. 26, 1947, after an injury in a wind tunnel at the National Advisory Committee on Aeronautics. He stated that

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From the Surgical Department, Elizabeth Buxton Hospital.

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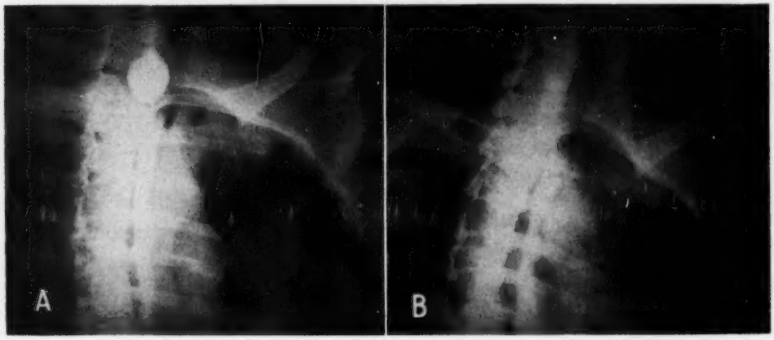
he had been struck about one hour previously by a blast of air from a compression air hose, the blast originating when a valve blew out about 3 feet (91 cm.) from his head, the blast being directed at his mouth, nose, head and ears (his eyes were protected by glasses). The initial examination showed swelling and bruising of the upper lip, with some cracking of the mucosa. The tongue was normal, and the teeth were in good condition. There were two large hemorrhagic areas on the soft palate. The pupillary reaction was normal to light and in accommodation, and ocular movements were normal. There was blood in the left tympanic membrane; the right ear was normal. There was no emphysema of the neck or chest. Examination of the chest showed it to be symmetrical, with good expansion and no dulness. There were harsh breath sounds and some musical rales. The heart was normal; the blood pressure was 122/84. Examination of the abdomen gave negative results. A provisional diagnosis was contusion of the upper lip, left external auditory canal and tympanic membrane and soft palate. Consultation with an otolaryngologist, Dr. George Hankins, was requested, and he found marked ecchymosis of the soft palate, hyperemia of the left auditory canal, loss of hearing in the left ear and normal sinuses. Urinalysis, blood count and Wassermann examinations gave normal reactions and a roentgenogram of the chest was negative. The patient was hospitalized for observation for three



A, roentgenogram showing diverticulum of the esophagus. *B*, roentgenogram six weeks after operation shows small amount of barium sulfate at level of diverticulum.

days and was discharged as improved. He was followed as an outpatient for one week and at the end of this time was discharged to return to work as cured. He returned on Jan. 27, 1949, complaining of substernal pain and dysphagia for four months, beginning shortly after his accident. He had not lost weight. An electrocardiogram was normal, as were roentgenograms of the chest. Blood and urine studies on February 1 showed no abnormalities. Roentgen examination of swallowing function showed a diverticulum of the esophagus (fig. 1 *A*). The patient was readmitted to the hospital on March 6, 1949. The past medical history and the family history were noncontributory except for the fact that his father had had tuberculosis. Physical examination showed a well developed 60 year old man who was not acutely ill, with a temperature of 98 F. and blood pressure 130/80. The breath sounds were normal, but the heart was slightly enlarged to the left. There were no abnormal findings. Examination of the neck disclosed no palpable masses. Urinalysis, blood count and Wassermann test showed nothing abnormal. On March 8 a first stage operation for removal of the diverticulum of the esophagus was done with the patient under nerve block and infiltration anesthesia induced with procaine hydrochloride. The diverticulum was exposed without difficulty and was found to be about 1 inch (2.5 cm.) long and ½ inch (1.3 cm.) in diameter. The esophagus was opened during operation and closed without further trouble. The wound was packed with petrolatum gauze and a Penrose drain inserted. The patient was treated with penicillin and got along well, his tempera-

ture rising to 100 F. on the second postoperative day. On March 15 (the seventh postoperative day), with the patient under local anesthesia, the diverticulum was removed without difficulty, the neck of the diverticulum being closed according to the method advocated by Lahey.[1] The patient had an uneventful recovery and was discharged from the hospital five days later. He returned for follow-up care, and swallowing function six weeks after the operation showed a small amount of barium sulfate retention at the level of the diverticulum as shown in figure 1 *B*. His subsequent course has been entirely uneventful.

SUMMARY

A case of esophageal diverticulum is presented, the precipitating cause being presumed to be a blast of compressed air.

INTESTINAL LIPODYSTROPHY (WHIPPLE'S DISEASE)

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AND
GEORGE M. RUGTIV, M.D.
DES MOINES, IOWA

THE RARE occurrence and infrequent recognition of intestinal lipodystrophy as described by Whipple [1] in 1907 appears to warrant report of a case diagnosed recently during laparotomy. The case reported by Whipple was characterized anatomically by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues. Clinically, the patient had recurring attacks of arthritis, emaciation, enlargement and tenderness of the abdomen and fatty diarrhea.

Since the original description of this disease, few reports have appeared in the literature.[2] To date the total number represents about 24 cases. The last case appeared in the literature in 1949, as reported by Copland and others.[2b] Several other authors have used the following terminology for this entity: lipophagia granulomatosis, lymphadenocele, mesenteric chyle adenectasis and lymphadenectasis.

REPORT OF A CASE

A 53 year old white man was admitted to the hospital in January 1950 with the complaint of dull aching pain in the left upper quadrant of the abdomen. This pain had been present since 1936 and had become progressively worse. It was described as deep in character, radiating to the lumbar region of his back. It was not associated with any food intake. At intervals he had mild diarrhea but recently had been troubled with progressive constipation. During this

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the results of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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period there has been no change in the character or type of stool; there was no history of fatty stools. He had maintained his normal weight and appetite. He had noticed a pressure sensation and a sensation of fulness in the epigastrium associated with an increase in the diameter of the abdomen.

The physical examination was essentially noncontributory except for a tender movable mass which measured about 10 cm. in diameter located paraumbilically and slightly to the left. There was no evidence of faulty fat metabolism on physical examination or on laboratory tests. The laboratory findings were within normal range. The liver function studies, including plasma serum protein, albumin-globulin ratio and cholesterol determinations, were normal. Examination of the stools on various occasions during hospitalization gave a negative reaction for carbo-

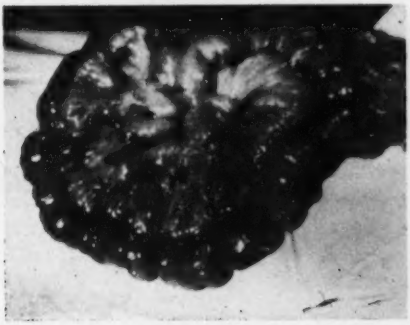

Fig. 1.—Photograph taken during laparotomy reveals thickening throughout jejunum and mesentery of small bowel, with areas of multiple fatty-like tumor masses.

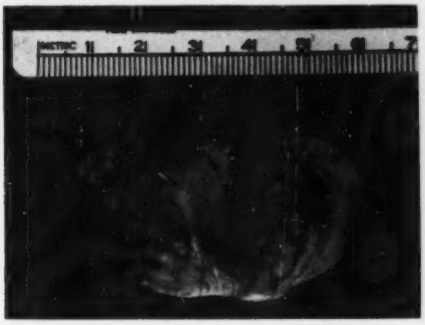

Fig. 2.—Gross specimen of one of the bright yellow, rubbery, fatty-like tumor masses.

hydrates and a 1 plus reaction for fats. There was no evidence of ova, parasites or blood in the stools on repeated examinations by microscopic and chemical studies. Roentgen ray examination of the gastrointestinal tract revealed no abnormalities of the esophagus, stomach, duodenum, small bowel or colon. The gallbladder was visualized and functioned normally. The roentgenograms of the lumbosacral region of the spine showed considerable demineralization of all the vertebrae. There were slight hypertrophic changes about the anterior and lateral margins of the lumbar vertebral bodies. Extensive calcification was noted in the aorta.

Gastroscopy and peritoneoscopy revealed no abnormal findings. Because of the presence of a palpable abdominal mass and unrelieved abdominal pain, an exploratory laparotomy was performed on Feb. 24, 1950. The entire mesentery of the small bowel was involved by fatty-like yellow-gray-appearing tumor masses (fig. 1). The mesenteric changes were present

from the root to the attachment to the small bowel. The mesentery and fatty masses were rubbery. In some areas the masses appeared separate and circumscribed, some measuring 2 to 4 cm. in diameter. Others appeared to extend in continuity with the thickened flat areas of the mesentery. There were no normal-appearing areas of the mesentery of the small bowel. The small bowel appeared slightly thickened throughout. The gallbladder, liver, colon, stomach, pancreas and duodenum were normal.

On their removal, several of the fatty-like tumors (fig. 2) appeared to be encapsulated and others seemed to blend in with the surrounding fat of the mesentery. Frozen section studies revealed fatty necrosis. In view of the extensive changes present, no operative procedure was attempted in regard to the mesenteric changes. Because of the complaint of abdominal pain, the splanchnic nerves were divided below the diaphragm.

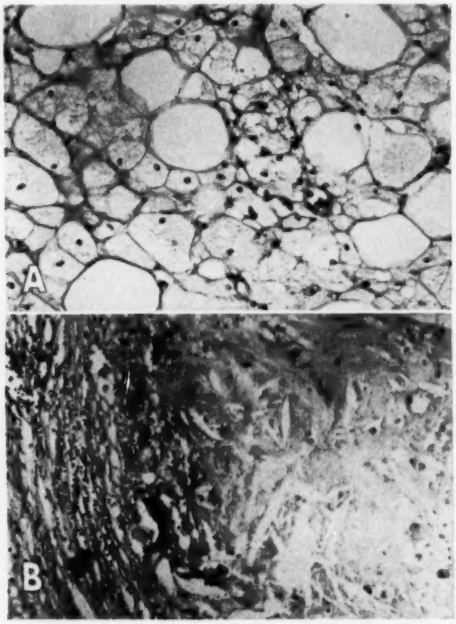

Fig. 3.—*A*, masses of mononuclear foam cells and large clear vacuoles representing fat droplets; *B*, area of fat necrosis surrounded by foreign body giant cells, lymphocytes and a zone of fibroplasia in mesentery.

The postoperative course of this patient was stormy as a result of pulmonary complications, elevation of the left dome of the diaphragm and atony of the stomach. At the present time his progress is satisfactory. His appetite is good, he is gaining weight and has no complaints referable to the gastrointestinal tract.

Pathologic Changes.—The specimen (fig. 2) was bright yellow and of a rubbery consistency. Multiple lymph nodes measuring up to 8 mm. in diameter were seen as opaque yellow nodules when the specimen was sectioned. A few larger, less sharply delimited nodules of fat necrosis were grayish white and were chalky in consistency.

Prepared sections of mesenteric fat contained focal and diffuse accumulations of damaged cells (fig. 3 *A*). These fat cells were polyhedral, with sharp cell membranes, slightly granular cytoplasm and small, centrally placed nuclei. There were infiltrations and peripheral accumulations of lymphocytes, plasma cells, neutrophils and a few eosinophils.

Foci of actual fat necrosis (fig. 3*B*) contained many cholesterol crystals (sharp angular clefts) and fine deposits of blue-staining calcium material. A few foreign body giant cells were present in these areas, and there was infiltration with lymphocytes, plasma cells and large mononuclear cells. Surrounding the areas of fat necrosis was a moderate amount of fibrosis, with the production of false fibrous connective tissue capsules.

In the lymph nodes from this tissue there was great retothelial hyperplasia. Focal accumulations of fat were seen, particularly in the retothelial tissue (fig. 4*A*).

Fat stains (sudan III; fig. 4*B*) confirmed the presence of intracellular and extracellular fat within the lymph nodes and the mesentery.

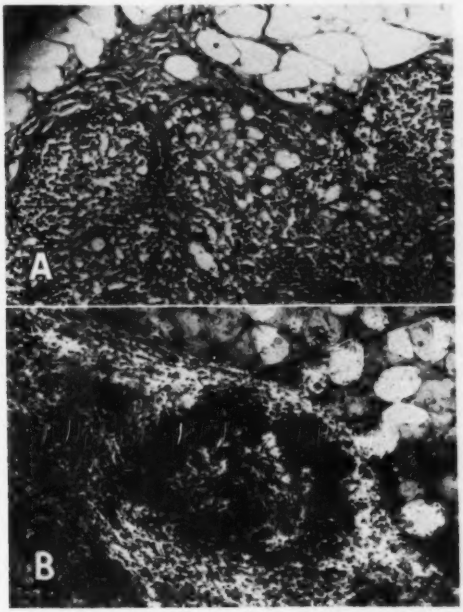

Fig. 4.—*A*, focal accumulations of fat cells in mesenteric lymph node; *B*, sudan III stain of mesentery to show zone of fat necrosis and the presence of intracellular and extracellular fat.

Because of the early stage of the disease, relatively few giant cells and dilated lacteal vessels were seen in this material. That explanation was proposed by Pemberton and others [2h] in their report of three early cases diagnosed at the time of operation.

COMMENT

The disease usually occurs most frequently in men between the ages of 40 and 60 years. Generally the complaints by the patient are bizarre and vague, usually, however, referred to the gastrointestinal tract. Flatulency, indigestion and indefinite pain in the upper part of the abdomen are complained of early in the course of the disease, and later, as the disease progresses, the patient suffers from fatty diarrhea, loss of weight, anemia, general debility and occasionally mild jaundice and pigmentation of the skin. The stools in the advanced cases reveal an excess of neutral fat and fatty acids.

Because of the indefinite complaints and lack of positive findings on physical, laboratory or roentgenologic examinations, the diagnosis up until 1945 was made at the autopsy table. Pearse [2g] in 1942 made the first antemortem diagnosis. Since that time the diagnosis in many cases and in our case has been made at the time of operation.

Since the original description of the pathology of the disease by Whipple,[1] little additional information has been added. Characteristically, the main pathological findings are limited to the small bowel and its mesentery. The mucosa of the jejunum and ileum is thickened and flecked with minute deposits of yellow-white lipid material. The mesentery is thickened, yellow and often nodular and has a rubbery consistency. The lymph nodes in the mesentery are enlarged and firm and on cut section often have a spongy appearance because of the dilatation of lymph sinuses. The lacteal vessels are often so dilated as to be seen grossly. On microscopic examination, the results of lymph stasis are seen, with dilatation of lacteal vessels and intranodal accumulations of fat. Degenerative changes are also often seen, as described and illustrated in this case, with the accumulation of large mononuclear foam cells, foreign body giant cells, lymphocytic infiltration and reactive fibrosis. The sequelae of stasis may or may not be actual fat necrosis. A similar picture is seen in the mucosa of the small bowel.

The etiology has not been established; however, many theories have been published. Jarcho [2e] feels that the disease is a result of a deficiency of pancreatic lipase, whereas Pearse [2g] states that it is a result of faulty bile metabolism. Apperly and Copley [2a] believed it to result from a failure of fat resynthesis, with a retention of fatty acids in the tissue. Glynn and Rosenheim [2c] theorized that there is an adrenal factor as the basic cause, whereas Reinhart and Wilson [2l] stated that it results from a malabsorption of fat. Hill [2d] contended that the disease results from obstruction of the thoracic duct and the mesenteric lymphatic vessels. At present there is no specific form of therapy. Most patients have a slow downhill course and die as a result of disturbed fatty metabolism.

SUMMARY AND CONCLUSIONS

1. A case of Whipple's disease, intestinal lipodystrophy, diagnosed at laparotomy is presented.

2. Whipple's disease is rare and has been reported infrequently since the original description in 1907.

3. The etiology remains unknown. The disease is characterized by faulty fat metabolism resulting in fatty changes in the mesentery of the small bowel.

4. There is no specific therapy. The majority of patients have a progressive downhill course and usually succumb as a result of faulty fat metabolism.

5. The pathological changes are characterized by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues.

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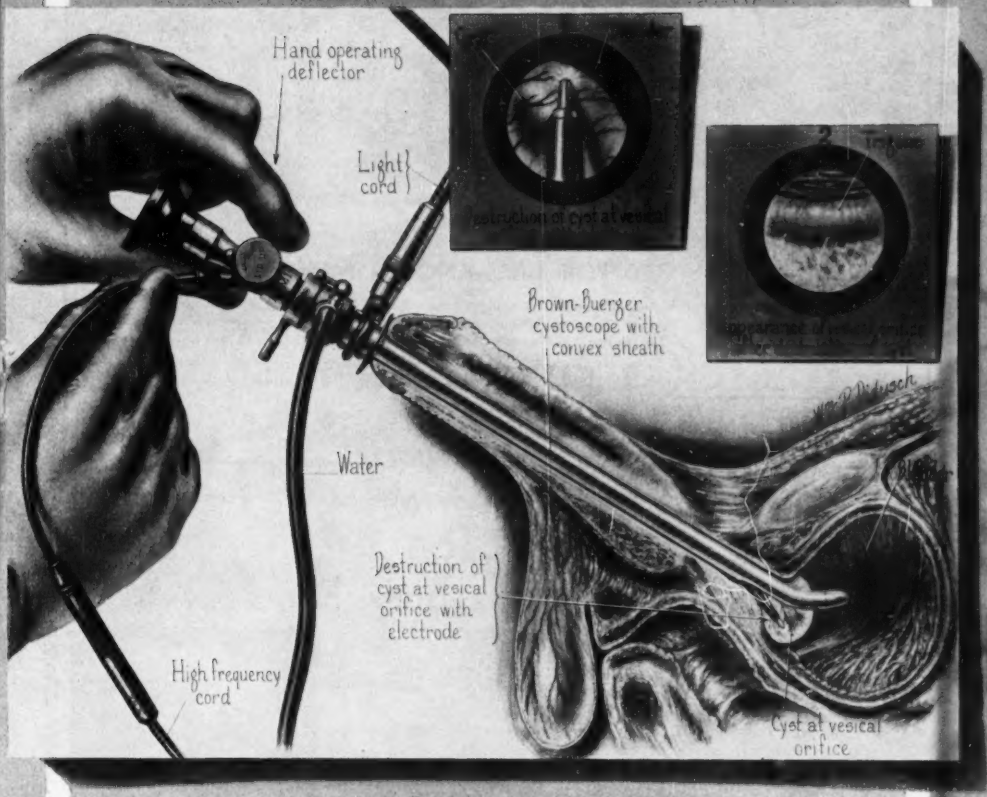

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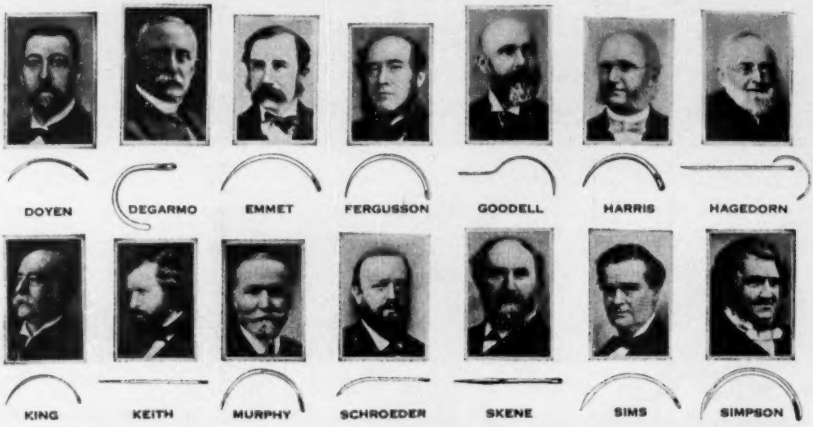

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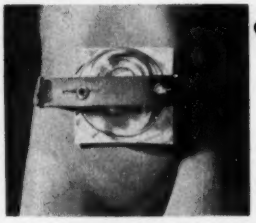

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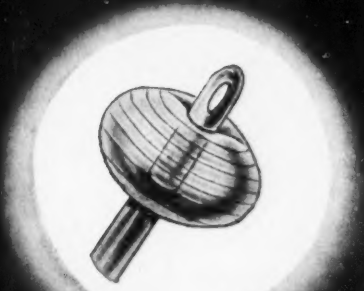

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